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THE ROYAL SOCIETY OF NEW SOUTH WALES

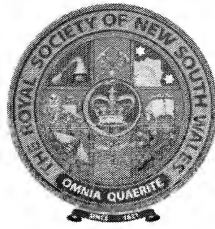
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Editorial

I write this editorial from the high plateau of the Atacama desert of Chile. In this extreme environment, the driest on our planet outside of Antarctica, the view out to the cosmos is superlative. Nations have been flocking to the *Altiplano* over the past decade to build instruments capable of giving us new insights into our universe, ranging from investigating how stars form inside cold, dense cocoons of dust in interstellar space – and then somehow engender planetary systems, to seeking echoes from primordial fluctuations in the microwave background radiation that pervades all of space.

When I am fortunate enough to set my telescope in operation, I am seeing a symphony in motion. The array of skills on display before me is truly magnificent – human insights into science and technology brought together in an engineering marvel that is a telescope and its instrumentation, all to allow me to seek faint signals from exotic molecules existing in environments which can barely be fathomed in the human experience, thousands of light years distant from us. When you have the privilege to conduct this orchestra, a masterpiece of the technological society we live in, it is hard to conceive that there is a parallel world out there where acceptance of science is waning, and belief systems rather than rational argument guide decision making for the human endeavour.

Yet that is the world we live in. Many of the great challenges we face as a civilisation, such as global warming and the

environment, require rational scientific thinking at their very heart to be tackled in a sensible manner. Increasingly, however, they are being given over to ideology and attacks on the scientific method that underlies our very understanding of them and our ability to address them.

This was the subject of the Society's Fellows Lecture this year, given by Distinguished Fellow Professor Barry Jones at the annual dinner. His lecture leads this edition, Volume 147–1 of the *Journal and Proceedings*. It heads a healthy content list, followed by Professor Brynn Hibbert's Mellor Lecture on the changing way in which scientists record their endeavours, and Nobel Laureate Professor Peter Doherty *in Conversation* with Society President Donald Hector. Then follows Council member David Branagan extolling the endeavours the Renaissance writer Georgius Agricola, and papers from three of the Society's student award winners for 2013: Jak Kelly award winner Xavier Zambrana-Puyalto on how to probe the nano-scale with light, and Society Scholarship winners Jessica Stanley on challenges in catalysis and developing sustainable processes, and John Chan informing us about the subject of biosimilars in medicine. I hope you enjoy reading these articles and sampling some of the worthy endeavours taking place today, guided indeed by the tenets taught us by the scientific method.

Michael Burton
Hon. Secretary (Editorial)
June 1, 2014





Evidence, Opinion and Interest – the attack on scientific method

2014 Distinguished Fellows Lecture

Annual Dinner of the Royal Society of New South Wales,
The Union, University and Schools Club,
25 Bent St, Sydney, 7 May, 2014

Barry Jones

AO, FAA, FAHA, FTSE, FASSA, FRSA, DistFRSN, FRSV, FACE

Abstract

Science and research generally are given disturbingly low priority in contemporary public life in Australia, although medical research and astronomy may be exceptions. Scientists, especially those involved with climate change, or the environment, have come under unprecedented attack, especially in the media, and the whole concept of scientific method is discounted, even ridiculed. In a complex world, people seem to be looking for simple solutions that can be expressed as slogans, and the quality of public debate on scientific issues has been trivialised, even infantilised. The controversy on anthropogenic global warming (AGW) has been conducted at an appalling level on both sides of politics. (Debates on refugees and taxation have been conducted at a similar level.) Vaccination, fluoridation and even evolution are hotly, but crudely, disputed in some areas. Despite Australia's large number of graduates (more than 4,000,000), our 38 universities and intellectual class generally have very limited political leverage and appear reluctant to offend government or business by telling them what they do not want to hear. Universities have become trading corporations, not just communities of scholars. Their collective lobbying power seems to be weak, well behind the gambling, coal or junk food lobbies and they become easy targets in times of exaggerated Budget stringency. Paradoxically, the Knowledge Revolution has been accompanied by a persistent 'dumbing down', with ICT reinforcing the personal and immediate, rather than the complex, long-term and remote. In a democratic society such as Australia, evidence is challenged by opinion and by vested- or self-interest. Australia has no dedicated Minister for Science with direct ownership/ involvement in promoting scientific disciplines. If every vote in Australian elections is of equal value, does this mean that every opinion is entitled to equal respect? It is easy to categorise experts as elitists, and out of touch. There are serious problems in recruiting science teachers, and numbers of undergraduates in the enabling sciences and mathematics are falling relative to our neighbours. In an era of super-specialisation, many scientists are reluctant to engage in debate, even where their discipline has significant intersectoral connections. Science has some outstanding Australian advocates, Gus Nossal, Peter Doherty, Ian Chubb, Fiona Stanley, Robert May, Brian Schmidt, Ian Frazer, Mike Archer among them, but they lack the coverage that is needed and that they deserve. There is a disturbing lack of community curiosity about our long term future, with an apparent assumption that consumption patterns will never change.

'The best lack all conviction, while the worst
are full of passionate intensity'

W.B. Yeats, 'The Second Coming', 1919.

What am I doing here?

I was Australia's longest serving Science Minister (1983-90), I think, in part, because nobody else wanted the job. Before and after that period I have maintained an intense interest in science / research and its implications for public policy and politics generally.

I have often been asked about how I came to be so heavily involved in Science policy and thinking about Australia's future, so let me begin with some personal reflections.

From childhood, I was deeply involved, obsessed even, in the history and philosophy of science and read HG Wells, JBS Haldane and Julian Huxley avidly. Jules Verne, too. These names, so important to me then, may be unfamiliar now. I tried to apply much of what I had learned about science in my political career, such as it was.

Despite having been a Member of State and Commonwealth Parliaments for 26 years, and a Minister for seven, I left politics with a profound sense of frustration and unease.

Political colleagues saw me as too individual and idiosyncratic, totally lacking in the killer instinct, while many in the academic community might have seen me as too political, even too populist.

My book *Sleepers, Wake!* was published by Oxford University Press in 1982, 32 years ago, and its success, both here and internationally, mystified and irritated many of my colleagues. It went through 26 impressions and was translated into Chinese, Japanese, Korean, Swedish and Braille.

Three decades on, my central thesis stands up pretty well. My major fault was in being too

cautious about the speed and impact of change. But in trying to predict the social, economic and personal impact of technological change, in 1982 I was Robinson Crusoe. I'll amend that in case you have not read Daniel Defoe: I'll say, 'I was on my own'.

Also, in politics, and in most other areas of life, nobody likes to be reminded: 'I told you so'.

In politics, my timing was appalling.

In October 1985 when I became the first, and, so far, only Australian Minister invited to address a G7 Conference, in Canada, the reaction of my colleagues was not celebration but irritation – 'Why him?'

I kept raising issues long before their significance was recognised. That made me, not a prophet, but an isolated nerd.

I can claim to have put six or seven issues on the national agenda, but I started talking about them 10 > 15 > 20 years before audiences, and my political colleagues, were ready to listen.

In politics, timing is (almost) everything and the best time to raise an issue is about ten minutes before its importance becomes blindingly obvious.

The issues were:

(i) Post-industrialism: the sharp decline in manufacturing as an employment sector due to the globalisation of markets and revolutionary changes in production techniques, leading to a sharp reduction in labour demand.

(ii) Information Revolution – transition to digital society / economy, with the development of low-cost personal computing, new ICT tools, and the development of the Internet, WWW and social networking.

(iii) Global Warming / Climate Change. I began talking about climate change, the impact of greenhouse gases and the human contribution to their production as Minister for Science, in 1984, so I have form in this matter. My timing – being far too early – was a major mistake. In March 1989 I spoke at a Conference in London, at the invitation of Mrs Thatcher, when Al Gore and I were the keynote speakers.

(iv) Antarctica. I argued for the need to preserve it for science, as a global climate laboratory.

(v) Biotechnology. I was fascinated by the implications of the DNA revolution and seized the opportunity to have discussions with some of the great figures in the genetic revolution, Crick, Watson, Perutz, Sanger.

(vi) Heritage. This involves trying to understand our history, places, environment and social context, and I worked on this area at UNESCO in Paris, on and off, between 1991 and 1996.

(vii) 'The Third Age.' The social, economic and political implications of the steady increase in longevity, especially since the 1950s, in which there has been a two and a half year increase in life expectancy for each decade of elapsed time. I worked on social policies for an ageing society in Cambridge in 2000 and 2001.

I was also heavily involved in securing the abolition of capital punishment in Australia,

reviving the Australian film industry and attempting to promote creativity in education.

My repertoire has been broad (even shallow) rather than deep and specialised. But I'm not bad at making connections – joining the dots', to use the current cliché.

The role of Science in policy development is a sensitive issue, because I have spent years, decades really, bashing my head against a brick wall trying to persuade colleagues to recognise the importance, even centrality, of Science policy.

Science and research generally are given disturbingly low priority in contemporary public life in Australia, although medical research and astronomy may be exceptions. Scientists, especially those involved with climate change, or the environment, have come under unprecedented attack, especially in the media, and the whole concept of scientific method is discounted, even ridiculed. In a complex world, people seem to be looking for simple solutions that can be expressed as slogans, and the quality of public debate on scientific issues has been trivialised, even infantilised.

Gus Nossal sometimes quotes me as saying that Australia must be the only country in the world where the word academic is treated as pejorative.

Many, probably most, of my political colleagues had no interest in science as an intellectual discipline, although they depended on science for their health, nutrition, transport, entertainment and communication.

When I was Minister for Science, one of my Caucus colleagues, who later succeeded me in that role, took me to a demonstration of a perpetual motion machine in his home state,

an invention which, he argued, would radically reduce the cost of living and manufacturing.

I saw the demonstration but was not persuaded.

My colleague was deeply disappointed by my scepticism. He asked why I dismissed the project. I said, 'Well, it can't be valid because it is in breach of the Second Law of Thermodynamics'. My colleague responded, 'We should repeal it.'

I was saddened that in all the tributes to Neville Wran in the past fortnight, there was no recognition of the five years he spent as Chair of CSIRO (1986-91). I took this as a confirmation of how far science has fallen off the political agenda.

As you are all well aware, currently Australia has no dedicated Minister for Science, although the title is a letterhead filler for the Minister for Industry. Research, including the ARC, is part of the responsibility of the Minister for Education, and the NH&MRC is under the Minister for Health. The recent National Commission of Audit characterised research as an expense, not an investment. The Commission might have regarded Wi-Fi, developed in the course of pure research by CSIRO, as a self-indulgent extravagance.

The lack of a dedicated Science Minister means that nobody in Government takes on personal ownership of science and acts as its advocate in Cabinet.

Science, Complexity and the Common-sense View of the World

There are major problems about explaining some of the issues in science, and has been ever since science began.

Some fundamental scientific discoveries seem to be counterintuitive, challenging direct observation or our common-sense view of the world.

Common sense, and direct observation, tells us that the Earth is flat, that the Sun (like the Moon) rotates around the earth and that forces don't operate at a distance.

Aristotle with his encyclopaedic – but often erroneous – grasp of natural phenomena, was a compelling authority in support of a geocentric universe, and that the seat of reason was in the heart, not the brain, and that females were deformed males. His views were dominant for 1500 years. The Greek astronomer Ptolemy, following Aristotle, provided ingenious proofs in support of geocentrism.

Then along came Copernicus, Galileo and Kepler who said, 'Your common sense observation is wrong. The orbits of the Sun and Moon are completely different, although they appear to similar.' (Our use of the terms 'sunrise' and 'sunset' preserves the Ptolemaic paradigm.)

By the 20th Century, electronics enabled us to use forces at a distance, do thousands of things remotely, manipulating spacecraft and satellites, or receiving signals (radio, telephony, television), setting alarms, opening garage doors and, one of the great labour saving devices, the remote switch for television.

The most obvious disjunction between science and common sense is the question: 'Right now, are we at rest or in motion?'

Common sense and direct observation suggests that we are at rest.

But science says, 'Wrong again. We are moving very rapidly. The earth is spinning on its axis at a rate of 1669 kph at the equator, and in Sydney (33.5°S) at 1388 kph. We are also orbiting round the Sun even faster, at nearly 30 kps, or 107,200 kph.

There are further motions, harder to measure, as the universe expands – and it's speeding up, as our Nobel Physics Laureate, Brian Schmidt, postulates.

But, sitting here in Sydney, it is hard to grasp that we are in motion, kept in place by gravity.

Psychology resists it – and essentially we have to accept the repudiation of common sense on trust, because somebody in a white coat says, 'Trust me, I'm a scientist.'

I would challenge anyone to reconcile common sense and quantum theory or to satisfactorily explain the Higgs boson or – hardest of all – to define gravity, although I suspect that Michelle Simmons could have made a credible attempt.

Scientific/ Analytical Method

Scientific method, rational analysis and evaluation of evidence has been a central factor in defining Western society and culture since the Renaissance, and these skills can be / should be applied to a variety of disciplines – politics, law, economics, social sciences, health. Scientists have come under unprecedented and damaging attack arising from the climate change controversy.

We must distinguish between scientific scepticism (a central element in testing evidence, for example Karl Popper's falsifiability test) and cynicism (dismissing evidence, however compelling, to promote confusion, inaction or vested interest.) Scientific vocations are falling in Australia,

and this has important implications for our future economic and scientific capacity. Governments have an obligation to take up and understand the challenges raised by science, reach a national consensus in promoting the importance of science in our national life, encourage investment in science-based processes and products for which there is international demand.

Political processes work on an assumption of common, or shared, knowledge – and this may be more fragile than we are prepared to recognise.

Robyn Williams of ABC Radio National's Science Show tells the horror story of addressing an audience of teachers – I should emphasise, not *science* teachers – some years ago when he asked, 'How many of you have never eaten food with DNA in it?' More than half the audience put up its hands.

The debate on climate change, especially anthropogenic global warming (AGW), has been a particularly disturbing illustration of how ill-equipped we seem to be in conducting serious debate and employing experimental method.

There are three areas of attack against expertise and taking a long term, analytical view of the world – from the Right, the Left and the anxious Centre.

From the Right there have been systematic and well-financed attacks by lobbyists from the minerals industry generally, especially coal and oil, and electricity generators. This has been highly personal, often abusive, sometimes threatening.

The anxious Centre includes people working in a particular industries and particular regions (Hunter Valley, La Trobe Valley, Tasmanian

forests), understandably fearful of potential job losses, without much prospect of creating new jobs. The trade union movement is deeply divided on this – as is the business community.

But from the Left, or some segments of the intellectual left, a deconstructionist mind-set has partly undermined an evidence-based approach to policy making or problem solving.

The pluralist or deconstructionist, or post modern, theory of knowledge is contemptuous of expertise, rejects the idea of hierarchies of knowledge and asserts the democratic mantra that – as with votes in elections – every opinion is of equal value, so that if you insist that the earth is flat, reject vaccination for children or deny that HIV-AIDS is transmitted by virus, your view should be treated with respect. Similarly, there has been a rejection of expertise and or taste – rejecting the idea of people like Harold Bloom, or me, that there is a ‘Western canon’ which sets benchmarks. No, say the deconstructionists, the paintings of Banksy, the mysterious British graffiti artist, are just as good as Raphael, that hip-hop performances are just as valid as Beethoven’s Opus 131.

Evidence vs. Opinion

There is a disturbing conflict between evidence vs. opinion (‘You have evidence, but I have strong opinions.’) and political processes tend to be driven by opinion rather than evidence in a short political cycle.

The Cambridge political scientist David Runciman argues that ‘opinion, interest and knowledge are too divided, and no event, whether an election ... or a crisis is clear enough in its meaning to bring closure’.

Creationism vs. evolution, the age of the earth (Genesis vs. geology), smoking as a cause of lung cancer, the safety of vaccination and fluoridation, whether HIV-AIDS is transmitted by virus, ‘alternative medicine’, controversies about the authorship of Shakespeare’s plays, the Kennedy assassinations, the survival of Elvis, even the historical truth of the Holocaust, are all examples of recent controversies which promote a confusionist mind-set and earn some people more attention than they deserve.

The Welsh geneticist Steve Jones asks an important question: If there is a division of scientific opinion, with 999 on one side, and one on the other, how should the debate be handled? Should the one dissenter be given 500 opportunities to speak?

Scientists are not immune from vanity, and some dissenters on climate change have been encouraged by being told: ‘The most important scientific factor in the climate change debate happens to be your area of expertise. Everyone else has it wrong. Only you are right’.

There has been a sustained attack from some quarters on scientific research and scientific method, even on rationality and the Enlightenment tradition. The illusion was created that scientists are corrupt, while lobbyists are pure. One of the false assertions is that scientists who take the mainstream position are rewarded, while dissenters are punished (similar to Galileo and the Inquisition). In Australia and the United States the contrary could be argued.

Scientists arguing for the mainstream view have been subject to strong attack by denialists who assert that they are quasi-religious zealots who are missionaries for a

green religion. In reality, it was the denialist / confusionist position to rely on faith, the conviction that there were a diversity of complex reasons for climate change but only one could be confidently rejected: the role of human activity.

The Infantilisation of Debate

Australia, like the US, UK, Canada and much of Europe, has undergone a serious decline in the quality of debate on public policy.

The British journalist Robert Fisk has called this ‘the infantilisation of debate’.

Just over 1,015,000 people (about 900,000 of them locals) are currently studying at Australian universities, both undergraduate and postgraduate. Australia has 4,000,000 graduates, far more than the total numbers of traditional blue collar workers. Inevitably these numbers will shift our political culture, but the process is occurring slowly. Members of trade unions amount to about one million people – 18 per cent of the total work force and about 12 per cent of the private sector.

Currently we are, by far, the best educated cohort in our history – on paper, anyway – but it is not reflected in the quality of our political discourse. We appear to be lacking in courage, judgment, capacity to analyse or even simple curiosity, except about immediate personal needs.

In the era of ‘spin’, when a complex issue is involved, leaders do not explain, they find a mantra (‘Stop the boats!’) and repeat it endlessly, ‘staying on message’, without explanation or qualification. The word ‘because’ seems to have fallen out of the political lexicon.

The killer punch against the Knowledge Nation Report produced in 2001 was the

notorious ‘complexity diagram’, all my own work. The decisive argument against the document was to say, ‘But it’s too complex’. Well, yes, indeed, that was the whole point of a complexity diagram.

An unexpected result of the ICT Revolution has been the development of social media, personal / self-referential, immediate, material, trivial – the smart phone as the ‘new best friend’, a love object in itself. ICT provides access to the universe with its astounding diversity, but observation of its users suggests that the personal has displaced the universal.

The eminent science writer James Gleick in his *Faster: The Acceleration of Just About Everything* (2000) calculated that in the United States the average time taken by a politician to complete his/her answer to a question on television was 8.2 seconds. I suspect that in Australia it would be longer – closer to 10 seconds.

There is fierce opposition in some quarters to the vaccination of children and the fluoridation of water supplies to prevent dental caries, even though the empirical evidence in support of both is overwhelming. But appeals to fear can be far more powerful than arguing on the basis of hard evidence.

Evidence-based policies and actions should be a central principle in the working of our system and reliance on populism and sloganeering should be rejected, but in reality they are not.

There was a very disturbing debate on climate change between Prof. Ross Garnaut and Clive Palmer on the ABC’s *Lateline* program on Friday 4 April, and you can view it for yourselves, if you can bear it, on YouTube. Ross Garnaut, an outstanding economist, was

author of the *Garnaut Climate Change Review*¹, an encyclopaedic work. But the debaters had no common ground. Prof Garnaut relied on evidence. Clive Palmer despite, or even because of, his vested interest as a coal miner, kept repeating the same mantra, over and over again, and never addressed the complex argument that Prof. Garnaut advanced. I suspect that many viewers, even late night viewers of the ABC, might have found Palmer's argument simpler to follow and to have been turned off by complexity, however compelling the evidence.

Tackling complex problems will demand complex solutions (e.g. refugees, climate change) which cannot be reduced to parroting a few simple slogans ('turn back the boats', 'stop this toxic tax'). 'Retail politics', sometimes called 'transactional politics', where policies are adopted not because they are right but because they can be sold, is a dangerous development and should be rejected. We must maintain confidence that major problems can be addressed – and act accordingly. Revive the process of dialogue: explain, explain, explain, rejecting mere sloganeering and populism. We need evidence-based policies but often evidence lacks the psychological carrying power generated by appeals to prejudice or fear of disadvantage ('They are robbing you...'). A voracious media looks for diversity and emotional engagement, weakening capacity for reflection and serious analysis, compounded by the rise of social media where users, typically, seek reinforcement of their views rather than being challenged by diversity.

Score Card

Australia ranks next to Norway on the United Nations' Human Development Index (HDI),

taking account of life expectancy, years of education and gross national income.

There is a long list of positives in our national history: democratic parliaments, free elections, probably the world's best electoral system (the Western Australian Senate poll in 2013 notwithstanding), pioneers of the secret ballot and universal suffrage, strong legal system with internationally respected courts, tradition of religious tolerance (although it could, in part, be indifference), secular education (but with some limits), good research (universities and CSIRO), excellent medical standards, superior public service, the ABC, courageous disaster relief.

But there are negatives as well: the long tradition of Aboriginal dispossession, burying their history, using them as quasi slave labour (and even worse), extraordinary rates of incarceration and domestic violence, brutality in the convict system (especially Norfolk and Sarah Islands) and the racism implicit in the White Australia Policy.

There has been a strong vein of authoritarianism in our system, often covered by the explanation, 'we are doing it for their own good', a rigidity, harshness, cruelty, even sadism in institutions – armed forces, churches, schools, orphanages. Churches, Parliaments, political parties, corporations, the media are all provoking community disquiet, with histories of corruption, suppression, secrecy and violence. The current Royal Commission about child sexual abuse presents evidence with a horrifying consistency. Treatment of asylum seekers shows unconscionable (but bipartisan) harshness. Vested interest is far easier to promote and secure than community interest.

We also have had a poor record in securing economic rights for women, discouraging

¹ Written in 2008; see www.garnautreview.org.au.

them from entering public life or the professions, our uncritical involvement in foreign wars and our acquiescence and credulity in the surveillance state.

Scientists and learned societies have been punching below their weight in matters of public policy, and they have advanced many reasons to avoid being involved in controversies outside their disciplines, the possible threats to grants being among them. We have distinguished scientists who are outstanding advocates, including Gus Nossal, Peter Doherty, Ian Chubb, Fiona Stanley, Robert May, Brian Schmidt, Ian Frazer, Mike Archer, Tim Flannery, Dick Denton being among them. Science must be at the core of our national endeavour and you are well placed to examine the evidence, evaluate it, then advocate and persuade. Our nation's future depends on the quality of its thinking, and its leaders.

I encourage you, whatever your political persuasion, or lack of it, to argue for higher recognition of the role that science must play in our future, and drive your MP mad unless or until he/ she does something about it.

Remember Archimedes and his lever.

But first you have to find a fulcrum, then you push the lever.

Sustained attacks on the mainstream scientific arguments for the need to take action to mitigate anthropogenic climate change have been from groups which could more accurately be described as 'confusionists', than 'deniers' or even 'sceptics'. The opponents do not analyse the evidence and advance alternate hypotheses which are themselves testable: their main goal is to promote confusion. To confusionists,

persuading citizens to conclude 'I just don't understand' is a very satisfactory outcome.

The international community readily accepted the argument that CFCs (chlorofluorocarbons) used as propellants in aerosol sprays were depleting the ozone layer, although their volume as a percentage of the atmosphere is infinitesimal compared to CO₂ and methane. This is in striking contrast to the combination of fury, hysteria and mendacity against the evidence of global warming. The explanation is that in the case of CFCs every chemical company was convinced that there were economic advantages in getting in first with HFCs (hydrofluorocarbons) as an alternative propellant, and that substitutes for CFCs could be adopted without economic dislocation and changes in consumption. But to much of the fossil fuel industry the global warming challenge is a fight to the death.

Publications by climate change denialists / sceptics mostly fall into two categories, knockabout polemic (mostly *ad hominem*) and objectors to a particular point of detail. The publications do not appear in refereed journals which suggests sharply alternative explanations – (i) that the material is not credible, testable or evidence-based, or, (ii) that there is a conspiracy by a scientific Mafia to suppress dissent. (Denialists are strongly drawn to the second alternative).

Both Whitlam and Keating emphasised the importance of high culture. Other than Malcolm Turnbull, nobody does now. There is a strong anti-intellectual flavour in public life, sometimes described as philistine or – more commonly – Bogan, which leads to a reluctance to engage in complex or sophisticated argument and analysis of evidence.

Paradoxically, the age of the Information Revolution, which should have been an instrument of personal liberation and an explosion of creativity, has been characterised by domination of public policy by managerialism, replacement of ‘the public good’ by ‘private benefit’, the decline of sustained critical debate on issues leading to gross oversimplification, trivialisation, the relentless ‘dumbing down’ in mass media, linked with the cult of celebrity, substance abuse and retreat into the realm of the personal, and the rise of fundamentalism and an assault on reason. The Knowledge Revolution ought to have been a countervailing force: in practice it has been the vector of change.

Media – old and new – is partly to blame. Revolutionary changes in IT may be even more important, where we can communicate very rapidly, for example on Twitter, in ways that are shallow and non-reflective. Advocacy and analysis has largely dropped out of politics and been replaced by marketing and sloganeering. Politicians share the blame as well, as consenting adults.

In the film *Wadjda* (2012), the first feature shot entirely in Saudi Arabia, directed by Haifaa al Mansour, a woman, the central character, an eleven year old girl with aspirations towards modernity and individual

expression, has set her heart on acquiring a bicycle, but this proposition arouses fierce opposition. In Saudi Arabia, it appears to be a known fact that girls who ride bicycles are incapable of bearing children. No evidence is provided but the opinion is strongly held. In the end, Wadjda gets her green bike but the difficulties she faced were comparable to those experienced by the director herself.

I have proposed my own variation on Pascal’s celebrated wager on the existence of God, set out in his *Pensées*, and applied it to climate change, as a way of evaluating the risk of global action vs. non-action about reducing greenhouse gas emissions:

- If we take action and disaster is averted, there will be massive avoidance of human suffering.
- If we take action and the climate change problem abates for other reasons, little is lost and the world benefits from a cleaner environment.
- If we fail to act and disaster results, then massive suffering will have been aggravated by stupidity.
- If we do not take action and there is no disaster, the outcome will be due to luck alone, like an idiot winning the lottery.



Experiences with LabTrove, a researcher-centric ELN: undergraduate possibilities and Twitter

Mellor Lecture of the UNSW Chemical Society Delivered on 9 May 2014

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Abstract

Electronic Laboratory Notebooks (ELNs) are progressively replacing the traditional paper books for recording of data and scientific reasoning in commercial research establishments and academic institutions, albeit not at UNSW Australia. The LabTrove ELN was designed and developed at Southampton University as an open source, web-based, recording system that is researcher-centric and can be tailored to meets the needs of individuals as well as entire research groups. The LabTrove system also ensures appropriate levels of security, and captures the meta-information necessary to establish reliable provenance. It is designed to promote cross-institutional collaborative working, to enable the sharing of procedures and results, and to facilitate publication.

LabTrove is being used in a heterogeneous set of academic laboratories around the world. At UNSW Brynn Hibbert's group has used, in part or in whole, this ELN. An Australian Learning and Teaching Council (ALTC, now OLT) grant allowed the development of a collaborative ELN for undergraduate analytical experiments. With the Universities of Sydney, Curtin, Chiang Mai (Thailand) and Southampton (UK) experiments were developed and tested that involved students from pairs of institutions, sharing data and interpretations but being assessed in their own departments.

As an example of the use of social media in chemical education, Twitter has been used as a channel of communication between lecturer and audience of 500 + first year undergraduate students. During the Mellor lecture feedback from the audience was solicited by a running monitor of a Twitter hashtag (#mellor2014) projected on a screen. Tweets from Sweden and other locations were accepted during the lecture.

1. Introduction

Professor David P. Mellor (1903-1980) was Head of the School of Chemistry at UNSW from 1956 to 1968, having spent 26 years at the University of Sydney, followed by 14 years as Professor of Inorganic Chemistry at UNSW. His research interests were mainly concerned with the properties and structures

of metal complex compounds. He also made considerable contributions to chemical education at the secondary and tertiary levels. David Mellor was President of the Royal Society of New South Wales in 1941.

Since 1960 UNSW has been active in developing new approaches to the teaching of chemistry within secondary schools through

its summer schools, the proceedings of which were published in the *Approach to Chemistry* series, including the commercially published *Chemical Data Book* (Blackman and Gahan, 2013). Using the royalties from these publications, the David Mellor Chemical Education Fund was established in recognition of the contributions made by Professor Mellor in the field of chemical education. The Fund is used to endow the Mellor Lecture and Medal. This Fund is administered by the University, with the involvement of the UNSW Chemical Society in the organization of the visiting lecturers.



Fig.1: David Paver Mellor (1903 – 1980).

Professor Hibbert was the first Mellor medallist from UNSW. A list of Mellor lecturers and medallists is given in Table 1.

2. Recording of Science

It may no longer be fashionable to discuss the Scientific Method, or even to explain it to our students, but it must form the basis of any approach to recording and disseminating

what we scientists do. The on-line Oxford Dictionary (Oxford English Dictionary, 2014) defines scientific method as:

“A method of procedure that has characterized natural science since the 17th century, consisting in systematic observation, measurement, and experiment, and the formulation, testing, and modification of hypotheses.”

Table 1: Mellor lecturers and medallists of the UNSW Chemical Society

Date	Lecturer	Institution
1972	L.E. Strong	Earlham College
1974	J.H. Wotiz	Southern Illinois University
1975	D.M. Adams	University of Leicester
1979	D.R. Stranks	University of Adelaide
1980	R.J. Gillespie	McMaster University
1981	A. Kornhauser	University of Ljubljana
1983	P.J. Fensham	Monash University
1984	P. Sykes	Cambridge University
1987	A.H. Johnstone	University of Glasgow
1995	C.A. Russell	The Open University
1998	T.E. Goodwin	Hendrix College
1999	B. Selinger	Australian National University
2003	S. Warren	University of Cambridge
2008	L. Sydnès	University of Bergen
2014	D. B. Hibbert	UNSW Australia

The results of the application of the scientific method are communicated to the world, and this is how we scientists are known. However from the start of the ‘formulation of

hypotheses' we need to document what we do. Not only to provide a historical record, perhaps one day for the Nobel Prize committee, or to establish our patent rights, or to ward off later investigations into scientific fraud, but to get our own thoughts in order and provide a narrative for our research.

The paragons of recording their science, according to Bird, Willoughby and Frey (Bird et al., 2013) and starting with Leonardo da Vinci, through Michael Faraday, Charles Darwin and Albert Einstein (and others) kept diary style notebooks. Paper was the only medium available, and paper was also the means for communicating with fellow scientists, either by personal letter or by publication in a learned journal. Data, obtained by observation and experiment, was also directly recorded in the notebook, as was information derived by analysis of that data. So Faraday had his notebooks, and indeed I had mine. I managed my three-year PhD with just two, and a third for theory.

Last year (2013) the School of Chemistry stores at UNSW issued 400 laboratory notebooks at a cost of A\$5600 which gives two to three books for each researcher per year. (About 130 PhD and honours were in the School in 2013).

Modern instrumental science, and this is certainly true of analytical chemistry, generates results at a great pace. Because of this, I believe it is evident that the trusty lab notebook has run out of pages to record all the data, and unfortunately we seem to have finished up with the worst of all worlds – we no longer can fit the reams of printed out spectra, graphs and so on between the blue covers, and of course cannot use them to store the 'raw data', but neither are we writing there the hypotheses, observations and

inferences that are the core of the scientific method.

To go from an experiment to what is revealed to a supervisor in a research group meeting is these days a long and drawn out process:

Instrument → raw data on instrument's computer → transformed data (proprietary software, spreadsheet) on student's computer → printed out graphs or transcribed numbers in student's notebook → and presented in PowerPoint.

What is finally shown by the student to her peers is highly selected (by the student) and not (easily) traceable to original results. Files on the student's computer are often not adequately backed up, or even decently indexed, and a consultation with the student can be a frustrating wait while folder after folder on their hard disk is searched through. A polite enquiry after, for example, a control experiment, can result in a panic trawl through files, or bland assurances that this has been done somewhere, and they will find it for you later.

Since the US Supreme Court passed rules accepting electronic records as equivalent to paper records in 2006, the headlong charge to the use of ELNs has been led by the patent juggernaut, which of course features many big chemical companies. In a review of ELN use, Phillips is quoted by Bird (Bird et al., 2013) as suggesting that the distinction between companies and academia is that large companies typically use ELNs to standardize quality control or establish a legal data trail; while academic labs use them to gain searchable access to, and then share, data. She identifies one of the greatest problems faced by an academic group is the turnover of personnel, resulting in an almost impossible task of retrieving data from only a few years

back. The ability to share data also has implications outside a group/ laboratory/ department/ university, more of which later.

2.1 Practicalities

In 2014 we are spoiled for choice. There are app ELNs, cloud ELNs, ones aimed at companies, ones aimed at data intensive research groups, and so on. In 2009 the analytical chemistry group of the School of Chemistry at UNSW started using the LabTrove ELN² because it was developed by a colleague and collaborator from Southampton University, Jeremy Frey, and he gave it to them for free. Luckily the company they spun out has thrived, and the product is still supported by academics.

But in 2009 not all the attendant and required technology was in place. When the School of Chemistry started using the ELN there were no real smart phones as such (the 2G Blackberry was all the rage) and certainly no tablet computers. Voice or even handwriting recognition software was hardly viable. The final killer, at the time, was the lack of a ubiquitous wireless network. So students tended to use the ELN off line, and while the physical cutting and pasting of instrumental output also must be done back in the office, there was never a wide uptake of the ELN.

Many of these issues are much improved, but the bottom line always appears to be the social and local political aspects, with resistance to change coming from all levels of a laboratory, from the students upwards.

Perhaps Bird and Frey got it right when they wrote last year: “Unfortunately the evangelists are frequently not the same individuals that will be creating the data and recording their work in the

electronic laboratory notebooks” (Bird and Frey, 2013).

(In the lecture delivered on 9 May 2014, a comment followed on proposals from the Australian Federal Government on the funding of higher education and the suggestion that the tertiary sector be deregulated. It is not reproduced here.)

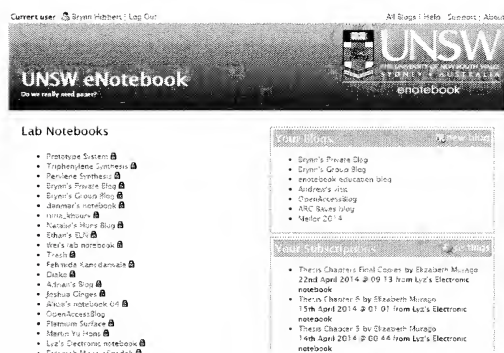


Fig. 2: The front page of the ELN used by the author's group. (Image taken 5 May 2014)

We left the direct scientific descendent of Michael Faraday, Brynn Hibbert, doing his PhD in London's King's College in 1973, writing in his lab note book without so much as a spreadsheet or printout. He visited the Royal Institution as Daniell (first professor of chemistry at King's College, and one of the founders of the delightfully named “Society for the Dissemination of Useful Knowledge”) would have visited Michael Faraday there. Not much had changed from a hundred or so years before, with data being largely recorded by hand. Sure he had spectra, assuming the ink in the pen of the chart recorder drawing out the trace had not congealed, but most data were measurements made point by point. The other aspect of science that had not changed was that communication was by physical letter, and publication by book and paper written for a journal.

² See <http://www.labtrove.org/> (Accessed 13 May 2014)

Now, in 2014, for scientists, publication in a journal (paper or on line) is still the preferred mechanism for enabling wider access to their material and providing the appropriate recognition for their work, although such publication does not constitute a full archival record, and many authors have pointed out the shortcomings of a paper-based mode of making scientific results available (Bartling and Friesike, 2014). Communication in general, though, is wider and faster, invariably electronic and often broadcast. With these possibilities for instant peer-to-peer interaction we have the decision to make about how open we will be with our ideas and knowledge. Indeed in a discussion (Gezelter, 2011) of the definition of ‘open science’ “... *the idea that scientific knowledge of all kinds should be openly shared as early as is practical in the discovery process*”, the point is made that journals are 17th /18th century technology for sharing scientific discoveries and today, we should be able to do better.

Much discussed in the literature is the ‘collaboratory’, defined in 1993 by Wulf as a: “... *centre without walls, in which the nation’s researchers can perform their research without regard to geographical location interacting with colleagues, accessing instrumentation, sharing data and computational resource, and accessing information in digital libraries.*” (National Research Council, 1993). To what extent this is achievable or desirable, may be debated, but it does now open up the discussion of the real role of the ELN, that of communication.

So I have finally arrived at my point. An electronic laboratory notebook has the capacity for immediate open access and sharing. There are many other benefits of security, metadata and audit trails, but in my view the possibility of throwing open the lab doors and allowing the world to help, is the most revolutionary aspect of the ELN, and

why no one feels they can go there yet, or at all. The School of Chemistry ELN can be set to allow access by everyone, no one or anyone. If we look at an ELN post, it allows comments to be added – very useful for the supervisor to comment on the fly, but this has much wider possibilities. Access is usually restricted to the immediate research group. When we set it up I (as group leader) hoped there would also be student-to-student interaction, and while there are some examples student-to-student posting has not become widely used. But wouldn’t it be nice if on posting the results of today’s experiments a comment appeared tomorrow from another group around the world with a new idea, or simply some encouraging words?

I cannot help but remember the Djerassi and Hoffmann play “Oxygen” (which I saw at an IUPAC General Assembly 2001) that explored the question “who discovered oxygen”? Every English scientist is brought up to know Priestley as the discoverer because of his work “Experiments and Observations on Different Kinds of Air”. But he visited Lavoisier (who named the new gas oxygen and worked out why it was not de-phlogisticated air) in 1774, only to receive a letter from Carl Wilhelm Scheele also describing experiments on the production of oxygen, but from the previous year. It appears communication between people came first (letters and visits) with publication somewhat later. The question of discovery may have been asked at the time (of course Lavoisier was soon busy having his head chopped off), but it seems now a modern fascination of who got there first, rather than why ‘there’ is important. The time it took to evolve Darwin’s “On the origin of species”, or in my field the posthumous publication of Bayes’ paper on “An Essay towards solving a Problem in the Doctrine of Chance”, suggested our forebears had understood the

importance of real communication, not just having another paper in the publication list.

And if you see where this is leading, the position of the formally-submitted and reviewed and published paper is perhaps under threat, as now being an obstacle to scientific progress. At one end the monograph or lengthy review article will always be needed, and at the other the Nature letter fantastic discovery is more and more electronic first anyway, but what of the interminable number of papers churned out after careful, or not so careful, peer review, simply to document the filling in of gaps in an evolving field? Is there a better way of compiling this knowledge, giving due credit to its originators, than in papers whose main text hardly has sufficient details to allow reproduction of the experiments, but more and more voluminous supplementary material is filling in some of the gaps. Do we have to have the formulaic introduction that is cut and pasted from paper to paper in a series, or the reference to a method that, if you can find it, turns out not to be able to be followed?

I argue that we now have the means to put in place these new, instant, modes of communication of science, and here I am just echoing people like Cameron Neylon and our own Matt Todd from Sydney.

I shall conclude this tirade with a quote:

“[the Review would urge]... all scientists to learn to communicate their work in ways that the public can access and understand; and to be open in providing the information that will enable the debate, wherever it occurs, to be conducted objectively.” (Russell, 2010)

Why this comment is significant is because it is from the Independent Climate Change E-mail Review, occasioned by some unfortunate language about scientific results in internal emails between climate scientists. That is, we

must always “show the working” (Hulme and Ravetz, 2009). I learned yesterday (8 May 2014) from Matt Todd, that they have lodged a copy of the relevant posts of an ELN as supporting information for a research paper that is being submitted for publication to a journal. The snapshot (once unzipped) can be browsed, and contains all the relevant experimental data from the original “live” electronic laboratory notebook (Badiola and Todd, 2014).

Finally, UNSW is not without its research scandals (thankfully not so many) and I cannot help but think experiments properly captured in an ELN might have saved, certainly the Faculty of Medicine, some pain.

3. Extensions and Additions

The LabTrove ELN used at UNSW (Fig. 2) is a web-based highly-linked blog, with layers of metadata. There is not much else to the basic blog page. Files can be attached, and now, through the ANDS-funded ACData project (Fig. 3) it is possible to blog results directly from instruments in the Analytical Centre and some electrochemical instruments in our labs.

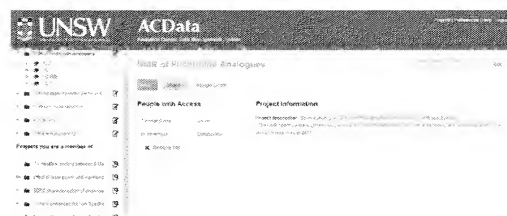


Fig. 3: A page from the UNSW repository of instrumental data, ACData. (Accessed 13 May 2014)

The original driver for this was to satisfy government archiving rules, but it also helps (forces) experimenters to organise their work (Project/ Experiment/ Batch/ Run), and naturally fits with the ELN concept. Those

who submitted ARC Discovery proposals this year might have wondered what the formula text was for the section “Management of Data”, which reads “UNSW has implemented a data storage solution for every stage in the life cycle of a research project”. Well, ACDData is a big part of this for chemistry, and using an ELN makes it easier.

Hopefully ACDData fulfils the observation of Huynh-Ba and Aubry “*On a practical level, a full electronic notebook, however desirable it may be, is not practical until all the instruments in a laboratory are computerized and networked.*” (Huynh-Ba and Aubry, 2000).

Accessed 19 May 2014 from: [http://www.chemspider.com](#)
Note: These links are not saved as part of your blog. Links are created when you edit your ELN entry. You can also fine-tune the suggested links.

ChemSpider Info

methamphetamine Confidence: 0.98
Hide ChemSpider data

Data collected on: 2014 05 05

ChemSpider url:
<http://www.chemspider.com/Record.aspx?cid=1169>
id: 1169
image
<http://www.chemspider.com/ImagesHandler.ashx?id=1169>
molecular weight: 149.2328
molecular formula: C₁₀H₁₅N
smiles: CC(C)CCCC(C)C
inchi: InChI=1.C10H15N.c1-9(11-2)8-10-6-4-3-5-7-10-h3-7.9.11H.842.1-2a3
inchikey: MYWUJZCMWCOHBA-UHFFFAOYAT
average mass: 149.2328
monoisotopic mass: 149.120453
nominal mass: 149.0
common name: Methamphetamine

References from Pubmed

[Show pubmed references](#)

- ☒ methamphetamine
- ☒ isopropanol
- ☒ water
- ☒ methamphetamine hydrochloride
- ☒ hydrochloride
- ☒ chloride
- ☒ p2a

[submit](#)

Query: methamphetamine AND isopropanol AND water

Title: Capillary zone electrophoresis (CZE) coupled to time-of-flight mass spectrometry (TOF-MS) applied to the analysis of illicit and controlled drugs in blood
Authors: Gottardo Rossella R. Department of Medicine and Public Health, Unit of Forensic Medicine, University of Verona, Verona, Italy; Polemi Aldo A. Soria Daniela D. Pascali Jennifer Paola J.F. Bortolotti Federica F. Liotta Eloisa E. Tagliaro Franco F.
(click to see, hide the abstract)

Fig. 4: ChemSpider and Pubmed information obtained automatically from an ELN entry containing the chemical ‘methamphetamine’. (Accessed 19 May 2014).

The ELN is evolving with new features such as time-line view, and the identification of chemical substances in each post. The latter was the outcome of a very nice project between Chemistry, the UNSW library and CSIRO. An ELN post turned out to be the ideal test bed for their developed software that falls in the class “semantic text miner and tagger”. A script is run once a day on the ELN to search for chemical key words in the text of any blog. When a substance is

identified the ChemSpider record is looked up and main data is displayed with link to the full record.

4. Undergraduate use of the ELN

In 2010 a consortium of ELN aware colleagues, from UNSW, University of Sydney, Curtin University, Southampton University and Chiang Mai University in Thailand, with UNSW as lead institution, put together a project proposal “Extending the science curriculum: teaching instrumental science at a distance in a global laboratory using a collaborative electronic notebook”. The goal of this project was to develop a framework for the incorporation of laboratory-based teaching into a global web-based undergraduate tertiary curriculum. The framework provides science educators with the tools necessary to implement an undergraduate course in the analytical sciences across two or more institutions, located within the same country or across international borders.

Unlike many web-based projects that focus on doing experiments at a distance we did not concern ourselves with how to control an NMR from the Moon, but on the peer-to-peer collaboration between students (and incidentally staff) in the context of an undergraduate lab. It was originally envisaged to be a series of five-way experiments, with one site actually performing the measurements and all sites receiving the data (via the ELN) and discussing, before individually writing up to satisfy their own assessment requirements. The vagaries of university terms (not so much time zones) meant this was never achieved, but quickly it was realised that this approach was most likely to be pursued in a one-university-to-university mode.

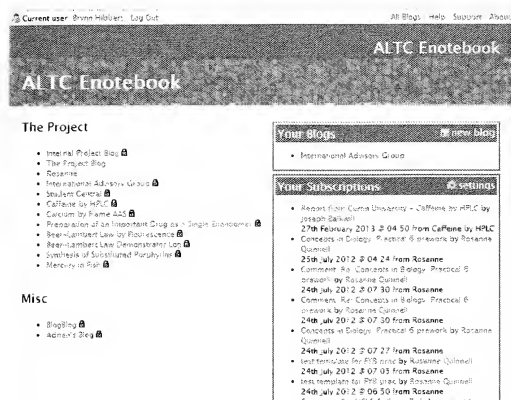


Fig. 5: ALTC electronic laboratory notebook.
<http://altc.oureperiment.org/> (Accessed 5 May 2014)

An unexpected bonus of the experiments developed for this project was the realisation that more traditional synthetic experiments may also be delivered via a collaborative web-based laboratory course. This can be carried out either by having local and remote students prepare analogues of the same basic compound, and then provide a collaborative interpretation of the data obtained. Alternatively the various cohorts can develop different approaches to a specific synthesis which is then collaboratively assessed to develop the “best” guidelines for synthesis. Matt Todd from the University of Sydney led this approach, and if you have not seen it, I would commend his open project to resolve the enantiomers of praziquantel, an effective drug against schistosomiasis (a water borne disease affecting some 200 million people) (Woelfle et al., 2011). The web site for the undergraduate ELN project can be found at <http://altc.oureperiment.org/>.

Experiments on the analysis of caffeine in drinks and mercury in fish are based on traditional laboratory experiments used at UNSW in a third year analytical chemistry course and provide examples of experiments that can be done at one location with the results loaded to the ELN and then used by

all. If several institutions that can measure mercury levels are involved in the course then obtaining data for mercury levels in different parts of the world becomes possible, with comparisons of results and resulting cross-cultural discussions.

This mechanism has the potential for helping developing countries at marginal extra cost to the host institution. Say a university like UNSW is doing an experiment requiring LC-MS-MS, an instrument not owned by Chiang Mai. In a collaboratory experiment, students at UNSW perform the experiment as they would normally do, but the results, raw data especially, are posted on the ELN for the group in Thailand. With the possibilities of high levels of interaction between the students, it is hoped that peer-to-peer mentoring happens without any fuss and the students in Thailand receive as authentic experience as possible without actually having the instrument in their lab.

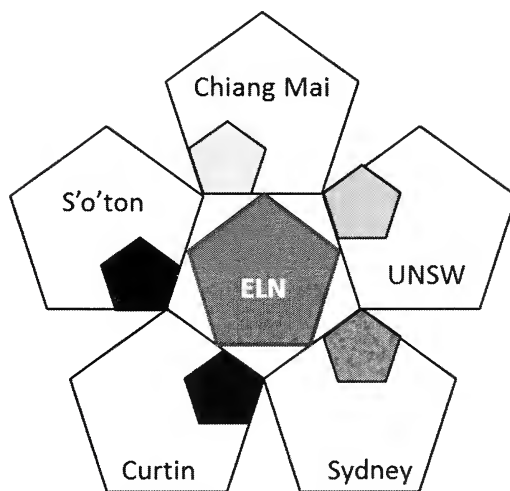


Fig. 6: Schematic of the electronic laboratory notebook (ELN) interacting with the five participating institutions.

Jeremy Frey from Southampton University offered an experiment to measure the extinction coefficient of an organic dye that

could actually be done over the internet, with a permanently running laser set up that could be turned on and fired over the web.

Although the development came at the end of the project we recognised that ACData could provide a long term and secure archive that can inform future courses. In quality assurance in laboratories, we use data collected over time to measure and monitor repeatability and reproducibility of results. In contrast in an afternoon of experimenting, when the students find themselves taking a standard deviation of three or four results, access to long run data allows a more authentic experience.

5. Social media in large lectures

Wikipedia lists 204 social networking sites headed by Facebook, Twitter, & LinkedIn, but then followed by Chinese and Russian sites the author has never heard of. As an aside, if the academic reader is concerned about the accuracy of Wikipedia, the author has just published a paper on the analysis of new synthetic cannabinoids (Lum et al., 2013) in which a table listing these compounds from Wikipedia is reproduced; this listing being far in advance of any official compilation. There are increasing opportunities for use of social media in research and education. Even the most staid journals these days invite you to 'like' them and their articles on Facebook. A new project on the social presence of IUPAC has just been approved. Headed by a Young Observer from last year's General Assembly in Istanbul, it has taken nearly a year to gain approval, perhaps because of a perception that such modes of communication are not necessarily for the peak International body in Chemistry. Yes they are.

The idea of using Twitter in chemistry at UNSW appears to have arisen simultaneously

between Marcus Cole and myself (Cole et al., 2013). The concept was to open a channel of communication to a group that was too large to interact with individually in the largest lecture theatre on campus (Clancy theatre with a capacity of over 1000).

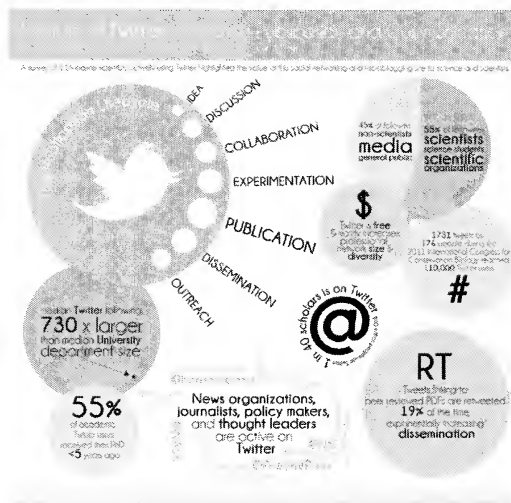


Fig. 7: Info graphic showing Twitter use in science communication. Reproduced from <http://visual.ly/twitter-and-science>, designed by 'KatiePhD' (Dr C.A. Pratt) <http://www.katiephd.com/>.

No student is going to put her hand up half way back in the Clancy to ask a perceptive question. With the hash tag #chem1011 and a Tweetdeck feed projected during the lecture, on the first day for some time absolutely nothing happened. I then asked anyone to tweet anything, to receive a question on how I first grew my beard. Once we had got that out of the way I asked them what was the last element that had been named by IUPAC? Quickly "Copernicus" came back, which I was reasonably happy with. We had just named Copernicium, element 112, so that was pretty good. When I explained the naming rules, a follow up tweet suggested that was what he had written but that the "spell checker changed it".

A year or so later we ran some surveys, using my own social network of psychologist Professor Jim Kehoe, and wrote up the paper that appeared in *J Chemical Education* in April 2013 (Cole et al., 2013). The usage was steady (about 10 tweets per lecture) without being overwhelming. About two thirds of tweets were about the lecture material or at least relevant to the course. The remaining third was an interesting mix of jokes, birthday greetings and general social glue. After the lecture, tweets followed up on questions. An interesting statistic was that only 23% of the class had a twitter account at the start of the project. (Present surveys in the US suggest it is over 80%). The bottom line showed 72% respondents in the survey thought Twitter helped learning, but there was some feeling that in the lectures it had the tendency to distract and intrude. Of course the Twitter feed can also be suspended or simply switched off, and used between lectures. Twitter, and other social media, is increasingly used by scientists to communicate and interact, among their professional communities and to quickly get their message out to the world. Fig. 7 is an infographic from 'KatiePhD' called "How Twitter can benefit scientists in terms of effects on publications, communication and outreach".

6. Conclusions

This paper has not been a hard sell for a particular electronic laboratory notebook. In writing this, the author has realised that whether UNSW Australia wakes up to the new technologies sooner or later is no longer the point. The world has advanced. What we do need to think about (as part of the discussion that is not happening either), are the kind of education and activities that should take place in a 21st century institution called a university, and how we expect our students to communicate the products of their scholarship and learning. I argue this

should not be just in their theses, or even papers for which their supervisors take equal credit, but in a continuous peer-to-peer exchange of ideas, data and knowledge, conducted, in part, through web-based tools.

So if I have in anyway stimulated or interested you, do not forget to like me on Facebook!

Thank you!

7. Discussion

The full discussion after the lecture is not presented here. The question that created the most debate came from Dr Jon Beeves (UNSW): "*Why would I give away all my unpublished results and allow others to publish it first to doom my career?*" There is genuine concern about groups, often in nations that are rapidly developing their scientific research, that 'borrow' ideas, and even data, from established sources in order to re-publish without acknowledgment. Dr Beeves argued that this would increase in an open science regime. The reply was twofold. First, plagiarism is as old as the proverbial hills, and increases with the amount of material that can be plagiarised. This is not the fault of open science. Second, making data and hypotheses available in an open source *is* publishing. Each post in an ELN is date and time stamped, and the source can be readily verified. This is more protected than a careless remark in a lecture at a conference, for example. So we are left with the concern that someone might 'stand on the shoulders of giants', by taking your results and then extracting the great idea of the age before you have had the same thought. Perhaps they might. A possible example of this scenario might have been the discovery of the double helix by Crick and Watson. We learn in "The Double Helix" (Watson, 1968) that Linus Pauling had theorised a triple helix, a structure that was instantly ruled out by the X-ray

patterns obtained by Franklin and Wilkins, and known only to Crick and Watson. Had these patterns been available to the world as they were obtained, it is possible that Pauling would have overleaped Crick and Watson to determine the correct structure. However the share of the Nobel Prize awarded to Maurice Wilkins (Rosalind Franklin having died in 1958) would still have been given for the data.

8. Acknowledgements

The photograph of Professor Mellor (Fig. 1) is reproduced from

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with permission of the copyright holder. The inspiration and information on open science and ELNs for much of the lecture comes from two papers written by Bird and Frey (Bird and Frey, 2013; Bird et al., 2013) and the many papers referenced therein. Fig. 7 is reproduced by kind permission of Dr Katie Pratt. The information in the graphic is based on Emily S. Darling, David Shiffman, Isabelle M. Côté, and Joshua A. Drew, The role of Twitter in the life cycle of a scientific publication, *Ideas in Ecology and Evolution* 6:32-43, 2013.

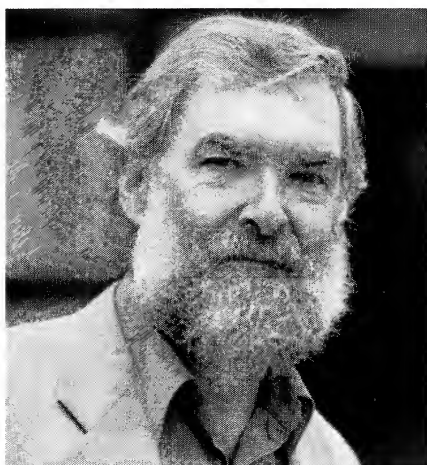
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In Conversation with Donald Hector

Peter Doherty

Laureate Professor, Department of Microbiology and Immunology, University of Melbourne
Distinguished Fellow of the Royal Society of New South Wales

Re-printed from "The Conversation", 12 May, 2014

<http://theconversation.com/in-conversation-with-donald-hector-full-transcript-26294>



<http://theconversation.com>

Abstract

RSNSW President Donald Hector interviewed by Nobel Laureate Peter Doherty for The Conversation on his views on science and technology in Australia, and the role for the Royal Society of New South Wales in promoting informed discussion on issues relevant to the well-being of society.

Peter Doherty: Thinking in terms of Australia's future, how important is it for us to expand activity in the innovation / high technology sector?

Donald Hector: It's critically important. If you look at countries that have been successful since the early days of the Industrial Revolution they've largely done so through having highly innovative industries that maximise utilisation of technology.

Peter Doherty: Do you think that an expanded high technology sector should focus solely on areas like IT, encryption, software development and so forth, or should we also be expanding niche manufacturing and both heavy and light engineering applications?

Donald Hector: It's all of the above. ICT is very important because there are enormous business opportunities in the industry; it's still very much in its infancy.

But it's also important to be developing niche operations and manufacturing capability in areas where Australia has a natural strength. Biotechnology and pharmaceuticals are a good example of that. Also industries that provide capability for areas where we are globally competitive such as mining and agriculture. And doing these on a world scale is also an opportunity that Australia has persistently overlooked.

There was a report commissioned by the government in the 1950s to take a snapshot of Australian industry immediately following the Second World War; pharmaceuticals are a really interesting case study.

We didn't really do much in the way of pharmaceuticals manufacturing at all until about 1948. We then started to manufacture penicillin. Australia was only the second country in the world manufacturing penicillin

commercially and was the first country to make it available for the general population.

We started making penicillin in 1948 and by the mid-50s we were one of the biggest penicillin producers in the world, if not the biggest. In 1950 the value of locally-produced pharmaceutical actives was £6.7 million and imports were £630,000. Over 90% of pharmaceutical actives used in Australia were manufactured in Australia.

Today the reverse is so. Over 90% of active pharmaceutical ingredients are imported, and the local content is largely limited to formulation and repackaging. We've gone from being in a very dominant position and self-sufficient position to an absolute devastation of that industry.

But it need not be like that. [Biotherapy company] CSL made the transition from government-owned enterprise to a highly-successful publicly-owned company, and is now one of the biggest producers of blood products in the world.

Tasmanian Alkaloids, which was started in Tasmania by Abbot Laboratories in the 1950s to produce opium alkaloids, was sold to Johnson and Johnson – why did this not end up in Australian hands?

Apart from a bit of generic pharmaceutical manufacturing in Australia we no longer make the medication that we need to treat chronic disease such as hypertension, diabetes and heart disease. If the supply of those were interrupted for some reason we'd be in a lot of strife.

Peter Doherty: What could the universities do better, both in the sense of discovery and translating discovery for economic benefit?

Donald Hector: I'm rather of the view that universities are best suited to doing pure research, and from time to time really good stuff will come out of that. But I think you need research institutions that are not constrained by a heavy requirement to produce income out of their research.

That's best left to private sector, and possibly government, and that's why I think the CSIRO and ANSTO [Australian Nuclear Science and Technology Organisation] are so important. They should be the commercial arms as was originally intended, and develop industrial research so that it puts Australia at the forefront of innovation.

Peter Doherty: What could CSIRO and other government research agencies like DSTO (Defence Science and Technology Organisation), ANSTO do better to promote greater economic activity?

Donald Hector: I'm not sure I'd include DSTO in that because they have very specific purpose.

I think CSIRO and ANSTO, and particularly CSIRO, are much maligned. They've created very innovative inventions over the years, and have been responsible for some truly fantastic technological developments.

But we expect them to deliver success with every project, and research is not like that. We also expect them to do so on shoestring budgets. There's nothing worse than funding a project that might be expected to cost \$50 million and finding out that it needs twice that, and then saying that you don't have the money to continue and killing the program. The reality of research and development is that if you think you've got a project \$50 million then you've at least got to have a couple of hundred in the pocket to take it

through, if you think once you get to \$50 million it's still got potential and that with more money it can deliver success.

I'm not suggesting that we should be trying to pick winners, nor am I suggesting that we should hesitate in killing off research programs that aren't going to deliver. There needs to be a very critical examination using some sort of stage gate process to do that. But you've got to make sure that you focus your funding on areas that are likely to be a success, kill off the programs in the early stages when they look like they're not going to succeed, and heavily fund the ones that show potential until they are successful, recognising that that usually takes a lot more money than you originally expected.

Peter Doherty: What are the barriers from the business side?

Donald Hector: We're not particularly good at managing risk in Australia. We're not particularly good at taking risks, nor are we good at managing them. What Australian companies, particularly the top 300 of the ASX, have historically done is to have very strong government lobby groups and the Australian governments, irrespective of their political persuasion, have been very heavily persuaded by them.

Historically, the argument was that Australia's not a big enough economy to have a fully competitive market place and so oligopolies and duopolies have been the flavour of the day. But that's no longer the case. We have a population of 25 million, we can have a fully open and competitive economy and there's more than enough room to have full competition without looking after these duopolies in the way that's been done in the past.

What I think that's led to is a lack of entrepreneurship. We lack a *mittelstand* in Australia of the type they have in Germany. I think there's three million smallish, family owned companies in Germany that typically have a few hundred employees and they're world leaders in a niche area. They supply world marketplaces and the big German manufacturing sector. We've never developed that here because we've been too eager to look after the larger companies that feel that the Australian government owes them a living.

Peter Doherty: Are we too risk-averse?

Donald Hector: I don't think we're risk averse – I think we don't understand the nature of risk. In managing risk you've got to be very skilled and have the capacity to understand the extent to which you know the ambiguities of situations and the likelihood or otherwise of success. That's very difficult. It requires a great deal of judgement and a great deal of experience. In Australia we tend to be fairly gung-ho and somewhat undisciplined, but the people I've met when I've worked overseas are generally people who manage risk well and are not risk takers. They know when to take steps and when not to take steps and they generally have very good business judgement. I think we often lack that in Australia.

Peter Doherty: Do we persistently under-invest?

Donald Hector: We often under-invest and then don't make sure that we get adequate return on the capital that we do invest. We often think that a project is going to cost a certain amount of money, and then when we get to the point where we've either run out of money and there's no more available or

people get cold feet and don't want to take it through to completion.

Peter Doherty: What can government do better? Are the tax settings right?

Donald Hector: I'm not sure that a general tax policy in terms of support for industry is a good idea. We certainly need research-and-development tax concessions. We need to have some public funding to encourage research and development expenditure, and we've got to recognise that issue and get a tax break on that.

I'm also of the view that if you're going to develop competitive industries you've got to have early-stage government support to do that. Virtually every major industry around the world is a consequence of government research programs, very often in defence sector.

If you look at the US, a lot of the industries there have their origins in defence industry. It's not uncommon to have in engineering faculties in the leading US universities to have hundreds of millions of dollars from government research funding for defence projects.

Australia could decide to be a much bigger player industries where we have some very clear internationally-competitive positions. For example in agriculture and mining, why aren't we more fully integrated into those industries? Why aren't we the manufacturers of agricultural and mining equipment as we were once?

Why was the government response to the car industry crisis not more visionary? We could have taken the several hundred millions of dollars of car industry subsidies and made that money available to a couple of the big

earth-moving companies like Caterpillar or Komatsu to establish their global research and development and world-scale manufacturing facilities here.

To me you need government policy to encourage the development of those industries, but you've got to do so in a way that will be internationally competitive and is going to develop an industry for the long term.

As occurs in countries like Singapore, and in the various US States, should government be actively pursuing financial and tax relief packages to persuade high-tech R&D to locate here?

I've been involved in one instance a billion dollar project that didn't get built in Australia, even though it would have been a good place to build, because there was too much bureaucracy from the federal government and the state governments to agree what sort of tax incentives and regulatory incentives would encourage investment. Eventually that plant went to China.

Peter Doherty: How do we encourage greater philanthropy, "angel investors" and so forth?

Donald Hector: I'm not sure that there's necessarily a place for philanthropy in developing technology, but certainly there is for angel investors.

One of the problems in finding angel investors in Australia historically is that there's just not enough private wealth here. But I think that's changing now because of the very great economic growth that's taken place in the last decade. My guess is that there's no shortage of angel investors if you've got good managers that they've got the risk of the

project under control, and they're good, professional, capable managers. We probably don't have enough experience of that here, so we're probably going to be relying on bringing people in from overseas, particularly the US, to manage start-up companies.

Peter Doherty: How important is it that we get a much better public buy-in to the idea that science and technology are important for our future?

Donald Hector: It's very important because science and technology nowadays are so complex that it's hard for lay people to really understand what the issues are. They get heavily influenced by special interest groups that might have an axe to grind about technologies coming to fruition.

I think we've seen this very much with issues like climate change where scientists have been vilified for speaking their mind and special interest groups are very quick to distort facts and throw misinformation into the debate to muddy the waters and pursue their own interests.

It's very important to have institutions there that can lead the discussion and make some of these things more readily available to the

general public and more able to have the information accessible.

Peter Doherty: What are you aiming to achieve by re-invigorating the Royal Society of NSW, and how do you see such long-established institutions functioning in modern Australia?

Donald Hector: We want the Royal Society of New South Wales to be true to its original charter of encouraging "... *studies and investigations in science, art, literature and philosophy* ...". The main aim behind that is to advance knowledge and encourage innovation and entrepreneurship to develop the resources of New South Wales and, more broadly, of Australia.

We see our role as providing a forum where we can bring together people who are interested in seeing those things happen and being a facilitator so that we can bring important issues to public attention and to influence policy. We want to provide a place for people to meet who are engaged in those areas of human knowledge, for them to exchange ideas and to learn from one another.



Signal to Noise Ratio in Renaissance Writing: an example concerning Georgius Agricola (1494-1555)

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Abstract

The modern term 'Signal to Noise Ratio' – a measure in science for comparing the level of a desired signal with that of its background noise – is used here with reference to the views of Adam Siber expressed in an elegy comparing the scientific and literary output of mediocre writers with that of Georgius Agricola (1494 – 1555). Written in Latin, much of Agricola's important work still remains untranslated into English, but his numerous works formed the basis of the understanding of many geological and mineralogical principles. The authors, in the process of translating one of his works – *De ortu & causis subterraneorum* – found the prefatory elegy which is also written in Latin. This paper outlines salient aspects of Agricola's life, including the social, 'scientific' and technological milieu in which he worked, and the influence on him of writers, both contemporary and ancient. This serves as background to our translation of Siber's elegy, wherein Agricola's communication skills are compared most favourably with those of lesser communicators.

Keywords: Agricola, Elegy, Siber, Hertel, Renaissance, Mining

1. Introduction

This paper has as its genesis the authors' foray into a translation of *De ortu & causis subterraneorum* (about the origin and causes of subterranean phenomena), a Latin work of Georgius Agricola (1494-1555). The volume from which we worked contains a prefatory elegy written by Adam Siber (1516 – 1584) and dedicated to Valentin Hertel (ca. 1500 – 1547). It, like most of Agricola's works, is written in Latin and we decided that it, too, deserves to be translated.

We chose the title – *Signal to Noise Ratio in Renaissance Writing* – because in our view this scientific phrase provides a most apt analogy for Siber's contrast between the clarity and significance of Agricola's works and the

ineffectual and often pointless efforts of lesser writers. The information torrent and its often irrelevant vortexes and eddies are not modern phenomena: the itch to impress ink on papyrus, palimpsest, parchment and paper has a long history, producing results of varying quality and utility in prose, poetry, philosophy, theology, engineering and science. Over against much fruitless and unoriginal work, any work of clarity, originality and utility stands out and persists as a work of distinction. In present day terms such relative measures are taken into consideration, even if largely unconsciously, when editors and reviewers rate a paper as worth publishing. In this paper we have taken the concept back to a time when publication was largely the prerogative of the writer himself (there were few female

authors). The Latin 'Elegy' by Adam Siber introducing Agricola's *De ortu* ... deals with this problem in considerable detail and calls on writers to be self-critical, even to the extent of withholding their work if it is not of sufficient quality.

This is the burden of Siber's *Elegy* written at a time of dynamic change: the Renaissance. Immersion in the classics of ancient Greece and Rome was considered essential to the standing and influence of learned scholars and this period produced prominent writers such as Erasmus, Thomas More and Rabelais, to mention but a few. It was also a time of religious turmoil: Martin Luther's Propositions drove a wedge among the Germanic people and, elsewhere in Europe John Calvin had initiated religious reforms.

Scientific thought grappled with three competing mechanisms of the recognised universe: the ancient geocentric view of Ptolemaeus; the heliocentric one of Copernicus and Kepler, and Tycho Brahe's geo-heliocentric compromise with the sun revolving around the earth and the other planets revolving around the sun. Educated elites believed in Aristotle's four elements of fire, water, earth and air, and all materials were believed to be mediated compounds of these basics.

Amidst this restless, developing intellectual milieu, Georgius Agricola researched and published works that laid the foundations of modern mineralogy. Siber's *Elegy* is a fitting paean to Agricola's intellectual rigour and painstaking observations, as it lists many questions the answers to which had previously been based on speculation rather than exact observation. Siber's praise of Agricola's lasting contribution to the body of knowledge of minerals resounds all the clearer when balanced against his persistent

condemnation of writing that is of no significant value. Indeed, Virgil's comment about Lucretius could justifiably be added to Siber's paean:

Felix qui potuit cognoscere causas.

Virgil (*Georgics*, 2, 4900)

[Blessed the man able to know the cause of things].

A translation of the elegy has in itself very little meaning – apart from justifying the title of the paper – unless it is prefaced by a brief summary of Agricola's life and work: the embodiment of clear communication. To this end, the first part of the paper describes his background; his achievements and the significance of his writings and researches in the development of the geological sciences. The translation itself presents the links between Agricola and many ancient written sources which he consulted and commented on in his works.

2. Agricola's Works (major and minor)

Georg Bauer, better known as Georgius Agricola (Figure 1), was the author of the well-known *De re metallica*, published posthumously in 1556. Although important for its text, this book's reputation is perhaps due largely to the fine woodcut illustrations which adorn the book and which have been widely reproduced. These woodcuts, showing technical mining devices, were prepared at St. Joachimsthal (now Jackymov), under Agricola's supervision. Skilled artists, led by Basilius Wehfring assisted by Rudolf Manuel Deutsch and Zacharias Specklin, prepared the mirror images for printing, all re-published in the first English translation by Hoover & Hoover (1912 and reprinted 1950) (Figure

2).³ Preparation of the illustrations delayed the original publication of *De re metallica* until shortly after Agricola's death (Lefèvre, 2010). It should be noted, however, that illustrations such as these were a common feature of the mining literature of the period (see for instance Urban (1980), Bork (2005)).

However Agricola was well respected during his lifetime for other important works on geological subjects, published much earlier, and essentially lacking diagrams, and this paper deals specifically with such a work.



Figure 1. Agricola, reproduced from Dibner (1958; original source unknown).

As quoted by Dibner (1958) Agricola wrote "Those things which we see with our eyes and understand by means of our senses are more clearly to be demonstrated than if learned by means of reasoning".



Figure 2. This illustration from Book VIII (Hoover & Hoover, 1912, p. 330) typifies the woodcuts which made Agricola's *De re metallica* famous. Here Agricola points to the 'reality' of the Argonauts' search for the Golden Fleece. In the water emerging from an underground stream (lower left – letter A) carrying material from a mineralised source a fleece is being used so that it traps gold particles. As the Hoovers point out Strabo gave a similar explanation centuries before Agricola did.⁴

In 1546 Agricola put together five separate works in Latin – one of which (*Bermannus* (1530, 1541) had previously been published (Michaëlis et al, 1971) – to form an important volume which we refer to as *Opuscula* ('minor works', which they certainly are not) because this is the title on the copy which is the source of our study. However the title *Opuscula* seems to be rarely used by other scholars, who refer instead to the volume in terms of one or other of the five separate 'essays' it contains (see for instance Morello, 2006).

³ The University of Sydney (Rare books) has an original copy

⁴ Glover (2003) noted this fact about the illustration.

In total this volume consists of:

1. Introductory Elegy
2. *De ortu et causis subterraneorum* libri V, first publication 1546, Basel; (pp. 1 – 82)
3. *De natura eorum quae effluunt ex terra* libri IV, first publication 1546, Basel; (pp. 85 – 164)
4. *De natura fossilium* libri X, first publication 1546 Basel; (pp. 167 – 380)
5. *De veteribus et novis* libri II, first publication 1546, Basel (pp. 381 – 416)
6. *Bermannus, sive de re metallica Dialogus*, first publication 1530, Basel (pp. 417 – 468)
7. Interpretatio Germanica vocum rei metallica addito [List of Terms (pp. 469 – 487; including the names of previous writers)]
8. Indice facundissimo [Unpaged Index 49 pages].

There were later Latin editions (essentially reprints: 1558, 1612, 1657), an Italian translation (1550), and a German translation (1806 – 1810) of *Opuscula*. There was no extended English translation of any part until 1955, when Bandy & Bandy (1955) published their translation of *De natura fossilium*, the third ‘essay’ in the volume.⁵ There is a modern translation of *Bermannus* into French (Halleux & Yans, 1990).

Although no English translations of the other essays have appeared, some of them have clearly been read, at least in part, by various English-speaking scholars, and their importance recognised, most notably by the Canadian geologist F.D. Adams (1938), who discussed some of the volumes’ main themes. Later scholars discussing the works include Eyles (1955) and Davies (1968), with fuller studies by Ellenberger (1988), Schmidt

(1995a), Morello (1994, 2006) and Mottana (2006); and brief comments by Oldroyd (1996). Eyles (1955) attributed the lack of recognition of Agricola as a pioneer of geology to the general neglect of the history of geology by historians of science, although this neglect has been reduced since Eyles made the comment. Following his detailed biography in 1956, Helmut Willisdorf continued leading the way with his editing, in association with W. Quellmarz, of *Georgius Agricola – Ausgewählte Werke Ergänzungsband 1*, Bergwerke und Huttenanlagen der Agricola-Zeit (Willisdorf and Quellmarz, 1971). In this work they deal specifically, inter alia, with Joachimsthal (pp. 157 and following), presenting information about the geology from recent research. Horst et al (1992) present the correspondence between Agricola and many associates, while H. Prescher (1994a, 1994b) has followed as the principal researcher on Agricola since the 1990s. The celebration at Chemnitz, in 1994, of the 500th year since Agricola’s birth, saw considerable research publications on his work, and this stimulated continuing studies. See, for instance Morello (1994), Vai and Cavazza (2003), Conolly (2005) and Vai and Caldwell (2006). Related publications includes Aldrich et al (2009). A major work is that of Neumann (1994), consisting of the papers presented at the Dresden meeting celebrating Agricola. The comprehensive list of works on Agricola, published between 1819 and 1977, prepared by Sarjeant (1980) is very useful, but is overwhelmed by the 1520 – 1963 bibliography (in German) by Michaëlis et al (1971).

⁵ Bandy & Bandy (p. 82) point out Agricola’s ground-breaking recognition of ‘mineralizing solutions’ [succus lapidescens] in the formation of mineral veins.

3. The Royal Society of New South Wales Connection

As far as we are aware the Royal Society of New South Wales holds the only book copy of this work in Australia.⁶ Although its source has not yet been traced an inked note on the flyleaf indicates it had been in French-speaking hands earlier. It was obtained by the Society some time prior to 1889, and has been re-bound and boxed (Branagan, 2007). The title *Opuscula* was possibly suggested by Archibald Liversidge of the Royal Society at the time the work was acquired by the Society and rebound.

With permission from the Society's then President, John Hardie, all the pages, including blanks (536 pages, containing only several 'formal' or decorative illustrations) were photographed in natural light, late 2010 – early 2011, with the assistance of Elizabeth Ellis (formerly State Library), and the Society's then Administrative Secretary, Brittany Cooper. Two missing pages were obtained later from Dr. Angela Kiesling (Bergakademie Library, Freiberg). Three copies were printed, with the view to translate into English at least some of the previously untranslated essays [to date the emphasis has been on *De ortu & causis subterraneorum*]; to examine their significance within the history of the Earth Sciences and to make the texts more readily available to English-speaking scholars. Our intention is to complete separate papers on some of these previously untranslated individual 'essays'. Some pages were quite difficult to work from as they did not reproduce well.

4. Available Sources concerning Agricola

Hollister-Short (2000) points out the paucity of studies by English-speaking researchers about Agricola, and comments that even much of the available work in English 'is seriously flawed', although space did not allow him to do more than point out what he regarded as incorrect in that respect. He suggested that the biography (in German) by Wilsdorf (1956) had been 'scrupulously researched'. Hollister-Short's brief review pointed to important aspects of recent research on Agricola's life, mainly in French and German. We have been able to access only a limited number of these publications to date, notably works by Wilsdorf and Quellmarz (1971), Michaëlis et al (1971), Horst et al (1992), so some minor points we make are open to revision. However some reviews in English indicate a growing interest in Agricola's works among English-speaking scholars (see, e.g. Hannaway (1992) and Beretta (1999)).

Other German language biographies of Agricola's life (notably Hofman (1905), and Hartmann (1953)) are useful, but there are only brief biographical essays in English. We have relied largely on Wilsdorf (supplemented by Prescher) in the *Dictionary of Scientific Biography*, 1985 vol. 1, 77-79; Hannaway (1992); Prescher (1994, a & b), the summary by Killy & Vierhaus (2009), but also Hoover & Hoover (1912, 1950) for the biographical information, although other sources, notably Horst et al (1992) have been useful for certain aspects of Agricola's life.

5. Agricola's Life: Social and Religious Context and Influences

Agricola was born Georg Pauer (Bauer) on 23 March 1494, one of four sons and three daughters of textile manufacturer Grigor

⁶ The University of New South Wales has a microfilm copy.

Pawer (his mother's name has not been identified) at Glauchau (on the right bank of the Mulde River, 12 km (7 miles) N of Zwickau, and 26 km (17 m) W of Chemnitz) (Figure 3 and Table). Zwickau is a district where there is strong mineralisation associated with a massive occurrence of serpentinite. Callenberg, a locality in that region, has been the site of recent (1952 to 1990) extensive mining of nickel occurring in a weathered serpentinite body. The region is also known for the occurrence of fine crocoite (lead chromate) specimens, first discovered at Ekaterinberg, Russia in 1786. Dundas, Tasmania, too, is known for its famous crocoite specimens.

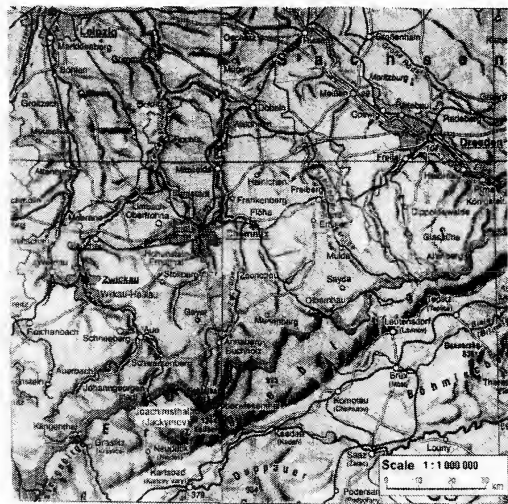


Figure 3. The Saxony region, showing localities related to Agricola's life [modified from Mitten in Sachsen pamphlet, Brand-Erbisdorf, Freiberg (n.d., ca. 1988)].

Of particular significance to Agricola's life was the turbulent religious environment in which he grew up. The long period of relative religious calm within the Holy Roman Empire was shattered by the upheaval caused by the thirty-three year old Augustinian friar and university professor, Martin Luther, when he posted his ninety-five propositions concerning the theory and practice of Indulgences on the

door of the University Church, Wittenberg on All Saints' Eve (October 31, 1517), when Agricola was just twenty-three. The consequent activities of the Reformation split the Germanic region in two.

Despite growing up in what became essentially a major Lutheran stronghold, and later working at times on diplomatic missions for the Lutheran Duke Maurice, Elector of Saxony, whose patronage he enjoyed, Agricola clung firmly to his Catholic faith, strengthened perhaps most notably by his long-term friendship with the scholarly humanist Dutch priest, Desiderius Erasmus (1466 – 1536), whom he probably first met in Bologna. It is a tribute to the tolerance of all involved that despite his firm adherence to 'Rome', Agricola maintained the respect and long friendship of many adherents of Protestantism. However his death was purportedly brought on by apoplexy, when arguing with a Protestant divine, and his site for burial became controversial.

In the early 1520s Agricola's travels took him to Italy, where, in addition to completing his training in medicine (doctorate awarded 1523, according to Beretta, 1999), he, like so many contemporaries, became aware of the rich history and culture of classical times. He also learnt something of the art of printing in Venice, particularly through being involved there in the editing of Galen's works for publication by the Aldine Press. This work gained the praise of Erasmus, who later proofread and recommended for publication Agricola's first mining study, *Bermannus* (1530).⁷

⁷ For a detailed discussion of Agricola's *Bermannus* see Morello (1994).

Table showing key events in Agricola’s life

1494	Georg Pawer (Bauer), born 24 March 1494 at Glauchau
1506	Bauer family moved to Chemnitz, attended Grammar school there
1511	Bauer family moved north to Magdeburg, Agricola schooled there
1514	Bauer enrolled at Leipzig University
1518	Graduated, moved to Zwickau, teaching, studying philosophy, published Latin textbook, possibly acquired the Latin name ‘Agricola’ at that time
1522	Returned to Leipzig, studying medicine, physics, chemistry
1522 – 24	Travelled to Italy (mainly Bologna/Ferrara), qualified as medical doctor
1524	Moved to Venice & Padua, worked on the publication of Galen’s work
1526	Returned to Zwickau
1527	Moved to Chemnitz
1527 – 1530	Moved to St. Joachimsthal (then a newly important mining centre), as medical doctor, began a detailed study (and recording) of mining
1530 – 1533	Travelled, (touring central European mining districts), but with residence at Chemnitz
1533	Returned to Chemnitz, remaining there, apart from short visits away
1546	<i>Opuscula</i> published
1555	Died 21 November, refused local burial; buried Schlosskirche, Zeitz (Halle), 45 km SW of Leipzig
1556	Agricola’s last work, <i>De re metallica</i> , published posthumously

1527 was a significant year when Agricola was appointed the town physician at St. Joachimsthal⁸ in Bohemia, on the south side of the Erzgebirge mountains (Figure 3). As Hannaway (1992) says, it was an unusual move for a Humanist, but it suited Agricola who was ‘concerned not with eloquence or rhetoric but with the recovery of knowledge’. The presence there of the humanist schoolmaster Petrus Plateanus (1505-1551), a Brabantine, provided a supportive friendship for Agricola. It was a newly flourishing mining town, where mining on a large scale began in 1516, producing mainly silver (Urban 1980), but the miners would probably

have puzzled over another ‘mineral’ present in the orebody. This was pitchblende, the radioactive substance which was to be the source for the important research by Pierre and Marie Curie in the 1890s (Curie et al, 1898).⁹ It is highly likely that some, at least, of the miners would have been affected by radioactivity, but there is no recorded indication that Agricola had any hint of this threat to the miners’ health.¹⁰ However in the

⁸ Silver from the Joachimsthal mines was the source of coinage that was named the ‘thaler’. This name was taken over by Dutch banks, and from this the word ‘dollar’ came.

⁹ Mme. P. Curie, (*Comptes rendus*, vol. 126, p. 1101) expressed gratitude to Eduard Suess, [1831 – 1914] ‘Correspondent of the Institute and Professor at the University of Vienna. Thanks to his benevolent intervention, we have obtained from the Austrian government the free gift of 100 kg of a residue from the treatment of the Joachimsthal pitchblende, containing no uranium, but containing polonium and radium. This gift will greatly facilitate our researches’.

¹⁰ For a surprisingly full detailed history of Joachimsthal mining history and the problems of radioactive minerals (including the discovery of uranium by Martin Klaproth

early pages of *De re metallica* ... while admitting that miners are sometimes killed by the ‘pestilential air which they breath’ or that ‘their lungs rot away’ Agricola gives a strong defense of the safety and value of mining.

At Joachimsthal (now Jackymov) Agricola began to take a serious interest in mining and geology during his leisure hours. He became friendly with Lorenz Wermann (ca 1490-1531/32), an earlier graduate from Leipzig, and an expert in metallurgy and mining who tutored Agricola (as probably also did Plateanus). Wermann soon appeared as the mining expert and protagonist Bermann in the Platonic-like dialogue *Bermannus sive de re metallica Dialogus* [*Bermannus or about matters metallic*] (1530), Agricola’s first foray into publications on geology and mining, which he reissued in 1541 and in *Opuscula* five years later. Three years were apparently enough for Agricola at Joachimsthal, and he travelled extensively again, gaining experience and knowledge on mining and geological matters before settling in Chemnitz. But there are few details of these times.

Probably following on from *Bermannus*, Agricola, in 1533, announced his intention to write a larger work on metals and mining technology (essentially what finally appeared as *De re metallica*). He had apparently been thinking about such a project in 1529, and might have already begun it. However it seems to have been put aside, or only worked on slowly while other publications appeared.

Ellenberger (1988, pp. 195-196) placed Agricola’s life in its regional and economic context:

the region of central Europe stretches from Bohemia to the Harz, embracing Saxony and Thuringia, at that time the richest in metal mines and the most advanced in mining technology. While the mineral concessions had belonged to the feudal rulers or to private capitalists, the mining communities had the use of franchises and considerable autonomy. ... The Saxon (s. lat.) miner was not a convict, but a man proud of his occupation, and whose competence was recognised throughout Europe. When one speaks of mines, one speaks also of interest in the reality of the underground. Now, differing from the Greco-Roman intellectual elite, Renaissance man began to integrate the best of practical knowledge into the higher levels of knowledge. The mining knowledge of central Europe (and just a little later, of Sweden) contributed, in a decisive fashion, to the birth of modern Geology, in particular causing the theoreticians to take into consideration that the underground was a developed framework, essentially a vast underground ‘architecture’ [our translation].

6. Relations with Contemporary ‘Scientific’ Authors

While Agricola was perhaps the best informed of the authors of the Renaissance who both studied and interpreted the works of ancient writers interested in mining and geology, he was by no means alone. However it is not appropriate in this paper to do more than touch on this subject. Suffice to mention only works such as *Pirrotechnia* (1540) by Vanoccio Biringuccio (1480 – 1538?) and the later *Treatise on Ores and Assaying* (1574) by Lazarus Ercker (1528 – 1594), which deals with matters similar to those discussed by Agricola in *De re metallica*, the last-named ‘justly regarded as a masterpiece of early technological writing’ (Hall, 1984). Also worth mention is *The Schwazer Bergbuch*, 1556, for which see Lefèvre (2010), where the colourful illustrations bear comparison with those of Agricola’s *De re metallica*. As Sprague de Camp (1963) points out, Agricola and

in 1789, its later exploitation and consequent health problems during and after WWII) see the internet site *Joachimsthal and pitchblende*, [h@g2, approved entry A1045 1099].

Biringuccio influenced each other, not an uncommon phenomenon then as now.

Dibner (1958) considered the difficulties met by Hoover & Hoover (1912, 1950), Bandy & Bandy (1955) and others in translating and understanding the many new Latin words coined by Agricola to name previously unnamed substances and mining terms, and to explain his ideas on numerous matters. The Hoovers had the advantage of a series of professional translators, and Herbert Hoover carried out laboratory experiments to test some of Agricola's statements (Lerud, 1995). The problems posed by Agricola's Latin were also considered in some detail by Morello (1994, p. 24). The major claim that Agricola was the first to put geology on a firm footing hinges on his abandoning speculation in favour of direct observation, as mentioned above.

7. Adam Siber and Valentin(e) Hertel, Source and Inspiration of the Elegy

The Elegy was written by Adam Siber to his friend Valentin(e) Hertel.¹¹ Siber (Siberius) (1516 – 1584) was born in Schönau, son of a First Reformed preacher, Stephan Siber, of that town. In 1546 Siber came from Halle to Chemnitz, and became an *Assistant* to Agricola. For a summary of Valentin(e) Hertel's life (ca 1500-1547) see Horst et al (1992). He was one of Agricola's younger friends, born at Glauchau, studying at Leipzig from 1515 and appearing as a disputant on the subject of the Triune God where he is noted as being a graduate of Leipzig.¹² He



Figure 4. Adam Siber. Source: Wittenberg Collection of Evangelical Preachers. No portrait of Hertel has been located.

was twice, over several periods, cantor of St Mary's Church, Zwickau, and teacher at the Latin school there. From 1539 he was Rector of the Latin School at Chemnitz where he is buried. Hoover & Hoover (1912, p. xiv) make a brief mention of letters Hertel wrote to the leading scholar Georgius Fabricius (1516 – 1571), author of the introductory 'poem' in *De re metallica*. Following Hertel's early death Siber became Rector at Chemnitz until 1559 when he moved to Grimma, dying there on 24 September 1584. Siber was also a friend of Fabricius, and is referred to as a humanist and pedagogue. He was a teacher and minor poet whose dedication to Hertel appears not only in the prefatory section of Agricola's *De ortu et causis subterraneorum* (1546) but also – in revised form – in his *Aeolostichon*, possibly written in 1550, and published in a collection of his works (1612). In translating the elegy we have occasionally turned to the revised edition (see Appendix) in an attempt to determine as accurately as possible the meaning of certain

¹¹ Hertel is not mentioned in any of the standard German biographical works such as Killy & Vierhaus *Dictionary* or Killy's *Literaturlexikon*.

¹² See the title page of *De Aere Theoremata Physica quae favente & fovente Deo Trium*, a debate between M. Georgius Gölner and Valentino Hertelio. Published Leipzig, 1620.

fairly abstruse couplets. Siber (Siberius) (Figure 4) is much better known than Hertel.

8. Siber’s Elegy and its Structure

In addressing the ‘Signal to Noise Ratio’ of this paper’s title we now consider and translate the introductory Elegy to Agricola’s *De ortu et causis subterraneorum*.

We are quite struck by the sentiments expressed by Siber, who was clearly an admirer of Agricola. Siber was apparently satisfied enough with the elegy to have it reprinted, with modifications, some years later with other of his poetical works, as mentioned above. In comparing Agricola with other writers Siber recognised the natural human desire to burst into print, but lamented the prevalence of psitticistic mediocrity in contemporary writing and rejoiced in Agricola’s original work.

Many earlier writers on bookishness and scribbling have decried writing that is obsessive, vainglorious, or lacking in lucidity; writing that is a vehicle for vanity and even an impediment to the spread of knowledge, motivated purely by vanity. Several such are quoted here:

qui de contemnanda Gloria libros scribunt, nomen suum inscribunt

[those writing books about the duty of despising glory, [don’t forget to] inscribe their own name (on the title page)]. [Cicero (*Tusc. Disp.*, 1, 15)]

Catullus, too, criticised the 10,000 lines written by Suffenus on royal papyrus:

neque idem umquam / aequae est beatus ac poema cum scribit / tam gaudet in se tamque se ipse miratur

[he is never so happy as when writing poetry, so much does he delight in and admire himself]. [Catullus 22: 15 – 21.]

The Latin elegy is a form that imposes considerable constraints upon the poet because of its metrical requirements: that is to say, it is to comprise a series of couplets each of which has the first line in hexameter and the second line in pentameter, with each pentameter consisting of two halves of two and a half feet each (see below). These criteria proved quite challenging to Siber with the result that several couplets seem clumsily constructed and, ironically, their meaning also consequently becomes by no means crystal clear. For these reasons our translation is a free one.

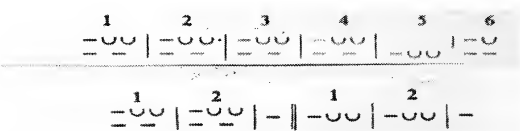


Figure 5. Latin Elegy metrical requirements

Siber’s Elegy – dedicated to Hertel – consists of forty-one couplets. The first fifteen directly relate to our title, *Signal to Noise Ratio*, in that the poet laments the proliferation of worthless works that produce nothing that has clarity and meaning. Couplets sixteen to nineteen list the requirements for good writing and express the hope that (like Agricola) Hertel will distinguish himself by producing, through diligent and painstaking effort, work that will justly earn him praise. The three following couplets offer a paean to Agricola whose work is rightly to be valued. Then couplets twenty three to thirty three introduce a list of the many contributions Agricola has made to the current body of knowledge of mineralogy. The couplets take the form of indirect questions and outline the many solutions to age-old questions that Agricola developed

through direct observation and careful recording.

Throughout this section, and indeed, through the entire elegy, Siber liberally resorts to literary allusions the better to illustrate how effectively Agricola demolishes mythical explanations for the earth's phenomena. There follow three couplets remarking on the lack of knowledge displayed by the eminent thinkers Theophrastus author of 'On Stones ...', Aristotle and even Pliny the Elder (a major source for Agricola), and then four couplets (thirty seven to forty) constituting an accolade to the value and deserved permanence of Agricola's work. The final couplet validates the choice of title for our paper: so much that it is worthless simply fades away, while Agricola's signal is received loud and clear.

Although such introductory poems are relatively infrequent in 'geoscience' publications, there are several such in Agricola's works, this one in *De ortu* ... and that in *De re metallica*. The Hoovers (1912) dismiss Fabricius' relatively long introductory poem to *De re metallica*, written in 1551, as 'of little intrinsic value' and 'not poetry of a very high order' and they simply reproduce it in Latin. However we believe that the elegy introducing *De ortu* ... is a legitimate object of study, and deserves translation and comment, being a window into the intellectual climate of the times, and showing many of the links between Agricola and his ancient sources.¹³

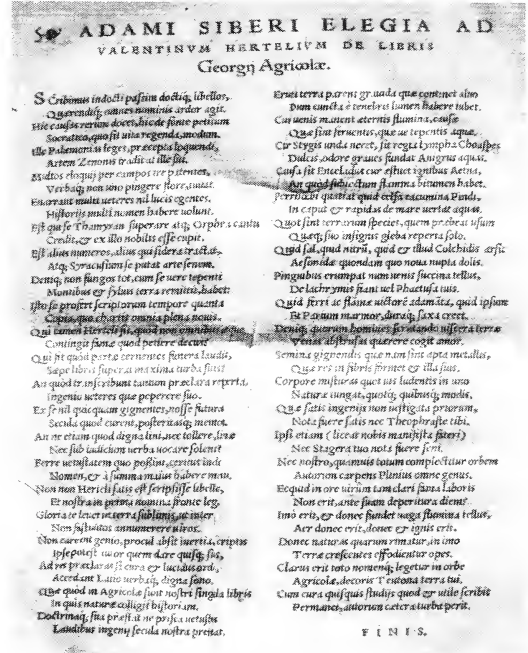


Figure 6. The Latin text of the Elegy (page 2 of our copy of *De ortu* ...)

¹³ Schmidt (1995a) lists some of the ancients which Agricola used. They include Aristotle, Theophrastus, Epicurus, Strabo, Seneca and Pliny the Elder; Arabic authors and mediaeval authors such as Dietmar von Mersburg, Elke von Repow and numerous contemporary writers.

9. A more legible form of the elegy

Adam Siberi elegia ad Valentinum Hertelium de libris Georgius Agricolae

- 1 Scribimus indocti passim doctique libellos,
Quaerendique omnes nominis ardor agit.
- 2 Hic causas rerum docet, hic de fonte petitum
Socratico, quo sit vita regenda, modum.
- 3 Ille Palaemonias leges, praecepta loquendi,
Artem Zenonis tradit at ille sui.
- 4 Multos eloquii per campos ire patentes,
Verbaque non uno pingere flore, iuvat.
- 5 Enarrant multi veteres nil lucis egentes.
Historiis multi nomen habere volunt.
- 6 Est qui se Thamyran superare atque; Orphea cantu
Credit, et ex illo nobilis esse cupit
- 7 Est alius numeros, alius qui sidera tractat,
Atque Syracusium se putat aete senem.
- 8 Denique non fungos tot, cum se vere tepenti
Montibus et sylvis terra remittit, habet;
- 9 Isto se profert scriptorum tempore quanta
Copia, quo chartis omnia plena novis.
- 10 Quid tamen Herteli fit, quod non omnibus aequae
Contingit famae quod petiere decus?
- 11 Quid sit quod partae cernentes funera laudis,
Saepe libris superat maxima turba suis?
- 12 An quod transcribunt tantum praeclara reperta,
Ingenio veteres quae peperere suo.
- 13 Ex se nil quicquam gignentes, nosse futura
Secula quod curent, posteritasque, memor.
- 14 An ne etiam quod digna lini, nec tollere, limae
Nec sub iudicium verba vocare solent?

- 15 Ferre vetustatem quo possint, certius inde
Nomen, et a summa maius habere manu.
- 16 Non non Herteli satis est scripsisse libellos,
Et nostra in prima nomina fronte legi.
- 17 Gloria te levet ut terra sublimis, ut inter
Non fastiditos annumerere viros.
- 18 Non careant genio, procul absit inertia scriptis
Ipse potest autor quem dare quisquam suis.
- 19 Ad res praeclaras si cura et lucidus ordo,
Accedant Latio verbaque; digna sono.
- 20 Quae quod in Agricolae sunt nostri singula libris
In quis [quibus?] naturae colligit historiam.
- 21 Doctrinaque sua praestat ne prisca vetustas
Laudibus ingenii secula nostra premat.
- 22 Eruta terra parens gravis quae continet alvo
Dum cuncta e tenebris lumen habere iubet.
- 23 Cur venis manent aeternis flumina, causae
Quae sint ferventis, quae ve tepentis aquae.
- 24 Cur Stygis unda necet, sit regia lympa Choaspes
Dulcis, odore graves fundat Anigrus aquas.
- 25 Causa sit Enceladus cur aestuet ignibus Aetna,
An quod subiectum flamma bitumen habet.
- 26 Perrhoebi quatit quid celsa cacumina Pindi,
In caput et rapidas de mare vertat aquas.
- 27 Quot sint terrarum species, quem praebat usum
Quaeque suo insignis gleba reperta solo.
- 28 Quid sal, quid nitrum, quid et illud Colchidis arsit
Aesonidae quondam quo nova nupta dolis.
- 29 Pinguibus erumpat num venis succina tellus,
De lachrymis fiant vel Phaetusa tuis.

- 30 Quid ferri ac flammae victorem adamanta, quid ipsum
Et Parium marmor, duraque saxa creet,
- 31 Denique, quorum homines scrutando viscera terrae
Venas abstrusas quaerere cogit amor.
- 32 Semina gignendis quae nam sint apta metallis,
Quae res in fibris formet et illa suis.
- 33 Corpore misturas quot vis ludentis in uno
Naturae iungat, quotque quibusque modis.
- 34 Quae satis ingeniis non vestigata priorum,
Nota fuere satis nec Theophraste tibi.
- 35 Ipsi etiam (liceat nobis manifesta fateri)
Nec Stagera tua nota fuere seni.
- 36 Nec nostro, quamvis totum complectitur orbem
Autorum carpens Plinius omne genus.
- 37 Ecquid in ore virum tam clari fama laboris
Non erit, ante suam deperitur a diem?
- 38 Imo erit, et donec fundet vaga flumina tellus,
Aer donec erit, donec et ignis erit.
- 39 Donec naturas quarum rimatur, in imo
Terrae crescentes effodientur opes.
- 40 Clarus erit toto nomenque legetur in orbe
Agricolae, decoris Teutona terra tui.
- 41 Cum cura quisquis studiis quod et utile scribit
Permanet, autorum caetera turba perit.

10. English Translation of Adam Siber's Elegy to Valentin(e) Hertel on the Works of Agricola

- 1) Learned or not we freely write books;¹⁴
The passion for celebrity drives us all.
- 2) One teaches the causes of things, another the Socratic¹⁵ way:
How our life ought to be directed.
- 3) Another propounds Palaemon's laws,¹⁶ the precepts of discourse;
But he passes on the arts of his mentor, Zeno.¹⁷
- 4) Many are delighted to pass through the fields of eloquence¹⁸
And to compose in a florid style.
- 5) Many, not lacking in esteem,¹⁹ expound the ancients;
Seeking a name in history books.
- 6) There's the lyricist who, with his crowing, deems himself superior to Thamyris²⁰ and Orpheus,²¹
And craves fame on that account.
- 7) There is one who deals with numbers – another with stars;
One who, indeed, regards himself a veritable Archimedes.²²
- 8) In point of fact one sees fewer mushrooms sprouting
In the spring-warmed earth of mountains and woods,²³

¹⁴ A direct quote from Horace, *Epistle* 2: 1, 117.

¹⁵ Socrates (469– 399 BC) wrote nothing himself, but his ideas have come down to us – however accurately – through his interpreters, Plato (c. 427 – 347) and Xenophon (c. 430 – c. 355 BC). His concern seems to be that intellectual investigation leads to happiness; 'the unexamined life is not worth living'. For footnotes on the ancients see Harvey (1937) and Howatson (1989).

¹⁶ Quintus Remmius Palaemon (fl. 1st century AD): grammarian and teacher at Rome under Tiberius and Caligula. An interesting account of him exists in Suetonius *De Grammaticis*, 23.1, 45–47.

¹⁷ A follower of Parmenides in the Eleatic school of philosophy, Zeno pointed out the paradoxical views on space and time held by the supporters of other philosophical doctrines.

¹⁸ The phrase '*per campos ire patentes*' occurs in Book 1, line 386 of *De Arte Poetica* (1527) by the Italian humanist and poet, Marco Vida (1485?-1566).

¹⁹ The phrase *nil lucis egent* appears in Bk. 6. of Vida's – *Christiados libri sex* (The Christiad in Six Books); we ponder Siber's originality.

²⁰ A legendary poet and musician who, in a contest at Delphi, won with his hymn in honour of Apollo. According to Homer, he met the Muses at Dorion and challenged them in song. In a jealous rage, the Muses deprived him of his gifts.

²¹ A legendary pre-Homeric poet whose lyre-playing held wild beasts spellbound by his music. In Hades he succeeded, by the power of his music, in having his dead wife, Eurydice, released but on the condition that he not once look back to see if his wife were following. Forgetting his promise his wife vanished forever.

²² Referred to as the Syracusan in this elegy, Archimedes (c.287 -212BC) was one of the greatest mathematicians (an astronomer and an inventor in physics and mechanics) of antiquity.

- 9) So great now is the plethora of authors
That the writers' world is weighed down by new works.
- 10) What is the point of it all, Hertel?
Hoped-for distinction eludes most of them.
- 11) What do we make of them demolishing established reputations
While complete confusion often dominates their own works?
- 12) Or that their 'distinguished' discoveries merely copy
Those the ancients achieved by their own ability.
- 13) Bear in mind they themselves are producing nothing
That future ages and thoughtful posterity would care to remember.
- 14) Though such works deserve to be erased
The authors regularly fail to hide them or submit them to criticism.
- 15) The pedants display their knowledge of antiquity
The better to be named by the most exalted writers.
- 16) Hertel, it is not good enough to have written books
Just for our names to be visible right there on the front page.
- 17) May distinguished work exalt you
To be numbered among men of reputation.
- 18) Such men should have talent and be diligent in their writings.
Such abilities are manifest in every leading authority.
- 19) If painstaking and methodical and writing in elegant Latin
They are equipped to engage with noble themes.
- 20) The fact is, all these qualities are characteristic of Agricola's works
Where he compiles an account of Nature.²⁴
- 21) So pre-eminent is his learning that
Sages' ancient doctrines do not eclipse current knowledge²⁵

²³ The revised version of the elegy (1612) clarifies the meaning of this and several other difficult couplets. Perhaps consideration of Virgil's *Georgics*, Bk II, 218 'ex se ipsa remittit' may validate our fairly loose translation. Perhaps, too, since fungus can have the meaning of dolt, Siber is saying that there seem to be more dolts than there are mushrooms in Spring.

²⁴ Siber may be suggesting that there is, among so many contemporary writers, no practice of ideas being submitted to critical discussion: what today we would call peer review.

- 22) As he sheds light on all those mineable substances
That Mother earth holds in her laden interior;²⁶
- 23) Why subterranean streams perpetually flow,
What the causes are of boiling or of lukewarm water
- 24) Why the water of the Styx²⁷ is deadly, the sacred Choaspes²⁸ sweet,
And why the Anigros²⁹ is malodorous;
- 25) Whether Enceladus³⁰ be the reason for Aetna's seething fire
Or whether the flame has bitumen in its thrall;
- 26) What shakes the high peaks of Thracian Pindus³¹
And turns rushing water from sea to river mouth;
- 27) How many are the kinds of earth, and what their uses,
Each sample has now its particular category;
- 28) What is salt, what is trona,³²
How did Medea³³ deceitfully set Jason's new bride ablaze,
- 29) Can the earth vent forth amber from her rich veins
Or is it made, Phaetusa,³⁴ from your tears?

²⁵ The revised version is different: *if anyone denies that these qualities reside in Agricola's works / Would you not think him lacking in judgment?*

²⁶ At this juncture Siber inserts in his later version a couplet not present in the text from which we are working: *And with Ciceronian phrasing he clarifies / What formerly was hidden out of sight.*

²⁷ In Greek mythology, the river Styx is the main river of the underworld. Here, it would seem to refer to a small river in what is now Chelmos. Men would swear oaths on its waters which were thought to have some deadly property.

²⁸ The Choaspes is a river remarkable for its pure water, said to be drunk by Persian kings. It is in what is now Kerrah (or Kerkhah or Kara-su).

²⁹ The Anigros is a river rising on Mauropotamo; its waters were muddy and unpleasant in smell.

³⁰ Enceladus was, in Greek mythology, one of a group of monstrous giants who attacked the gods and were defeated. As punishment, they were imprisoned in the earth. In the case of Enceladus, he was confined under Mt Etna.

³¹ Pindus is a lofty mountain in Thessaly close to the reputed home of the Muses.

³² Trona is a native hydrated double salt of sodium carbonate and sodium bicarbonate, occurring especially as an evaporite.

³³ Medea is referred to as Colchis after the province Colchis in Asia, east of the Black Sea: the setting for the story of Jason and the Golden Fleece. When Jason rejects Medea and takes another wife, Medea uses her magical skills to create a cloak which – given as a present to the new bride – bursts into flames as soon as it is placed on the wearer. In this elegy, Jason is referred to as Aesonides, a descendant of Aeson. In the legend, Medea had earlier used her magical potions to restore youthful vigour to Aeson – Jason's aging father.

³⁴ Phaetusa was, in Greek mythology, the daughter of Phoebus and sister of Phaeton. When Phaeton crashes to earth after losing control of his father's chariot, his body is finally found by his mother and his sisters, one of whom is Phaetusa. She and her sisters weep so profoundly over his body that, as they lie on the ground, they are transformed into trees. Their distraught mother tears at the trees in an effort to release their bodies causing drops like blood to trickle from the wounds. The bark closes over the wounds, hardening the tears into amber (Ovid, *Metamorphoses*, Bk. II, 330-366).

- 30 How flame and iron produce the conquering steel;
What brings about hardy rocks, especially Parian marble.³⁵
- 31) Natural strong interest in such matters
Drives men to examine Earth's interior, seeking mineral veins:
- 32) What are the essentials for generating metals;
What substances form in stringers and what seeds them;
- 33) How many compounds does capricious Nature combine in one body
By however many and whatever possible ways;
- 34) These matters, not sufficiently traced by the intellects of the ancients
Were not even known adequately to you, Theophrastus.³⁶
- 35) May we be permitted to speak the obvious?
Nor were these things known to your old Stageran³⁷ himself.
- 36) Nor, in our time were they known to Pliny³⁸
Although he embraces the whole world, grazing over every type of author
- 37) Surely the reputation of [Agricola's] so distinguished a work
Will not perish in the sight of men before its time.
- 38) On the contrary, his reputation will endure
As long as the earth's rivers flow, as long as there's air and fire.
- 39) As long as he examines the nature of these phenomena
Increasing riches of the earth will come from deep below.
- 40) Famous he will be and, through the entire world,
The name of Agricola – your adornment, oh Teuton land – will be read.
- 41) One who cares for scholarship, writing what is useful, survives;
Mediocre scribblers sink without trace.

³⁵ Parian marble is found in Paros, one of the Cyclades, and is renowned for its beauty and fineness. Paros (now Paro) was the birthplace of the poet Archilochus.

³⁶ Theophrastus (c.371-c. 287 BC) was a pupil and friend of Aristotle and his successor as head of the Peripatetic school of philosophy.

³⁷ Here, Aristotle is referred to as Stagera, a town in Macedonia where he was born.

³⁸ Pliny the Elder (23 or 24 – 79 AD) was a man thirsty for knowledge. His greatest achievement is the *Naturalis Historia* in thirty seven books, dedicated to the future emperor Titus in 77. He perished in the great eruption of Vesuvius in 79. His nephew, Pliny the Younger, wrote an account of his uncle's fatal trip to investigate the smoke coming from the mountain.. See also Holland (1962). The phrase 'our times' is perhaps used by Siber to distinguish AD writers from those of the BC era.

11. Conclusions

From our own translations of both Agricola's *De ortu & causis subterraneorum* (a work in progress) and Siber's elegy, the authors have formed the strong conviction that Agricola was an outstanding applied scientist who had a coherent vision and a clear *modus operandi*. In every age there are learned people of such ability as to rise above the scribbling crowds peerlessly and effortlessly and to be justifiably esteemed. We found Siber's elegy of great interest because - like other dedicatory elegies - it reflects the thoughts and attitudes of a key part of the subject's audience: friends and supporters. Within the lines, one detects a strong exhortatory tone: Hertel should emulate Agricola's rigor and clarity if he wishes to attain lasting recognition. Of particular interest is the fact that Siber chooses to underpin his paean to Agricola and his work with a condemnation of communication characterised by anything that makes a work obfuscatory: vainglory, carelessness, or plagiarism. For this reason we consider the scientific term Signal to Noise Ratio an appropriate title for this paper: Agricola's signal is received loud and clear.

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Appendix: Siber's Revised Version of the Elegy (c. 1550)

Scribimus indoctri passim doctique libellos,
Quaerendique omnes nominis ardor agit.

Explicat hic rerum caussas: hic fonte petitum
Socratico, quo fit vita regenda, modum:

Ille Palaemonias leges: praecepta diferti
Zenonis pressa monstrat at ille manu:

Eloquii multos per campos ire patenteis,
Verbaque non uno pingere flore iuvat:

Enarrant multi veteres, nil lucis egentes:
Historiis multi nomen habere volunt:

Est qui se Thamyran superare, atque Orphea cantu
Credat et ex illo nobilis esse cupit:

Est alius numeros, alius qui sidera tractat,
Atque Syracusium se putat arte senem.

Denique non fungos tot, cum se vere tepenti
Montibus et sylvis terra remittit, habet:

Se profert isto scriptorum tempore quanta
Copia, quo libris omnia plena novis.

Quid tamen Herteli, quid fit, non omnibus aequae
Ut veniat famae, quod petiere, decus?

Non raro partae cernentes funera laudis,
Et superet libris maxima turba suis?

An quod transcribunt tantum praeclara reperta,
Ingenio veteres quae peperere suo?

Nil ex se quidquam gignentis, nosse futura
Secula quod curent, posteritasque memor.

An ne etiam, quod digna lini nec tollere, limae
Nec sub iudicium verba vocare solent?

Ferre vetustatem quo possint, certius inde
Nomen, et a summa maius habere manu.

Non satis, Herteli, non est scripsisse libellos,
Indicet ut titulum pagina prima tuum:

Gloria te levet ut terra sublimis, et inter
Non fastiditos ut numerere viros:

Non careant genio: procul absit inertia scriptis
Ipse potest autor quem dare quisque suis;

Ad res praeclaras, si curo et lucidus ordo,
Accedant Latio verbaque digna sono.

Quae neget Agricolae monumentis si quis inesse,
An non iudicio iure carere putes?

Agricolae, qui nunc praestans ne docta vetustas
Laudibus ingenii secula nostra premat:

Ingressus terrae latebras, Plutonia regna,
Audax, naturae perficit historiam.

Et Ciceroneo sermonis lumine, clara,
Occultata prius quae latuere, facit.

Aeternis manent cur venis flumina, caussae
Quae sint ferventis, quaeve tepentis aquae.

Cur Stygis unda necet, sit regia lympa Choaspes,
Dulcis odore graveis fundant Anigrus aquas.

Caussa sit Enceladus cur aestuet ignibus Aetna:
An quod subiectum flamma bitumen habet.

Perrhoebi quatiat quid celsa cacumina Pindi,
In caput et rapidas de mare vertat aquas.

Quot sint terrarium species, quem praebeat usum
Quaeque suo insignis gleba reperta solo.

Quid sal, quid nitrum: quid et illud, Colchidos arsit
Aesonidae quondam quo nova nupta dolis.

Pinguibus erumpat num venis succina tellus,

Illa fluant lachrumis an Phaetusa tuis.

Quid ferri ac flammae victorem adamanta, quid ipsum
Et Parium marmor, duraque saxa creet.

Denique quorum hominess scrutando viscera terrae,
Venas abstrusas quaerere cogit amor:

Semina gignendis quatenam sint apta metallis,
Quae res in fibris formet et illa sui

Corpore misturas quot vis ludentis in uno
Naturae iungat, quotque quibusque modis.

Quae satis ingeniis non vestigata priorem
Nota fuere satis nec Theophraste tibi.

Ipsi etiam (liceat nobis manifesta fateri)
Nec Stagera tuo nota fuere Sopho.

Nec nostro, quamvis totum complectitur orbem,
Autorum carpens Plinius omne genus.

Et fore quis putet, ut tam pulchri fama laboris
Obscura ante suum fit peritura diem?

Non ita: sed donec fundet vaga flumina tellus,
Aer donec erit, donec et ignis erit:

Donec naturas quarum rimatur et ortus,
Quas gignit tellus effodientur opes:

Clarus erit, toto nomenque legetur in orbe
Agricolae, decoris Theutona terra tui.

Cum cura, studiis quicumque quod utile, scribit,
Permanet: autorum caetera turba perit.

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Probing the nano-scale with the symmetries of light

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Jak Kelly Award Winner, 2013

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Abstract

An alternative approach to study light-matter interactions in nano-photonics is presented. This method is based on considering light and sample as a whole system and exploiting their symmetries. The mathematical formalism to systematically study symmetries of light beams is explained and particularly applied to vortex beams. Then, the method is used in two different problems. First, it is shown that vortex beams can be used to effectively turn any dielectric sphere into a dual material. Then, it is seen that the same light beams can be used to excite whispering gallery modes on free space, thus avoiding the evanescent coupling typically used in these kinds of problems.

Introduction

In 1959, Richard Feynman gave a seminal lecture entitled “There’s Plenty of Room at the Bottom” which pushed scientists to set out on the journey of controlling light-matter interactions at the nano-scale (Feynman, 1960). Since then, nanotechnology has rapidly developed. Nowadays it is unconceivable to think of any new information devices whose circuits are not nano-metric. Whereas nanoelectronics is a well-consolidated technology producing transistors of less than 30nm, nanophotonics has yet to overcome some drawbacks to be fully competent. One of the most important ones is overcoming the diffraction limit of light. Most of the efforts in this direction have been happening in the field of plasmonics. In fact, lots of authors consider that nanophotonics should be based on metallic nano-plasmonics (Brongersma, 2010). Plasmonics is the science that studies the interaction between light and free electrons on a metal (Maier, 2007). The first

theoretical studies in plasmonics were done in the 1950's (Bohm, 1951; Pines, 1952; Bohm, 1953; Ritchie, 1957), and the first experimental realisations in the 1970's (Otto, 1968; Kretschmann, 1971). Since then, the field has successfully expanded and nowadays its applications have spread over many different fields (Lakowicz, 2006; Atwater, 2010; Juan, 2011). In general, plasmonics uses a sample-based perspective to overcome the diffraction limit of light. That is, given a fixed incident beam, samples are engineered (shape and materials) so that the desired light-matter interaction takes place. Fig. 1 shows the intensity profile of a typical incident beam used to excite plasmonic structures. A beam of light with such intensity profile is known as Gaussian beam, since its intensity profile can be described with a 2-dimensional Gaussian function (Pampaloni 2004). Now, there is no doubt that precise fabrication and characterization of samples play a huge role in designing the current plasmonic technologies. Interestingly, the spatial profile of the incident

beam is also a key factor in the light-matter interaction.

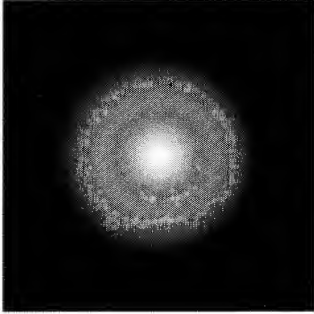


Figure 1: Intensity profile of a Gaussian beam. The intensity is maximum in the areas coloured in yellow, and minimum in those coloured in black.

However, most of the work in the field is done with Gaussian beams or plane waves. In this article, it will be shown that more elaborated beams of light can be used to retrieve plenty of additional information from nano-structures. An illustrative example is the Stimulated Emission Depletion (STED) microscopy. STED microscopy was invented by Stefan Hell and co-workers in 1994 (Hell, 1994). It is one of the so-called super-resolution microscopy methods, as it can resolve defects as tiny as 30nm (Rankin, 2009; Rittweger, 2009). Its working principle is detailed in Hell (1994, 2007), but the main idea is the following one. Probing a sub-wavelength specimen with a Gaussian beam results in a blurry image. Nevertheless, the combined use of a Gaussian and a doughnut-shaped beam results in a much neater image. That is, the use of a doughnut beam turns out to be crucial in order to overcome the diffraction limit of light. There are different kinds of doughnut-shaped beams, but the ones used in STED are called vortex beams (Molina-Terriza, 2007; Yao, 2011). Vortex beams are defined by their optical charge l , which is an integer number. The optical

charge l accounts for the number of times that the phase of the beam wraps around its centre in a 2π circle. As an example, four different vortex beams are shown in Fig. 2. It can be seen that when $l = -1$, the phase goes from 0 to 2π one time in counter-clockwise direction. In contrast, when $l = 3$, the phase goes three times from 0 to 2π in a clockwise direction. Currently, vortex beams are mostly experimentally generated with Spatial Light Modulators (SLMs). Check Bowman (2011) and references therein to see how vortex beams are generated and what their principal applications are.

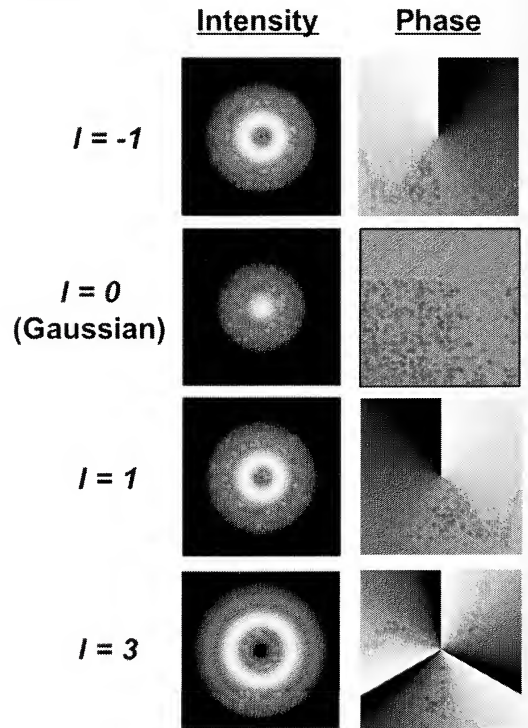


Figure 2: Intensity and phase profiles of vortex beams with optical charges $l = -1, 0, 1, 3$ respectively. For the intensity plots, yellow indicates maximum and black minimum. For the phase, white means 0 phase, and black means 2π .

Note that the definition of a vortex beam and its optical charge are independent of the

polarisation. However, for many applications in nano-photonics (STED microscopy is one of them), vortex beams need to be tightly focused. When that is the case, vortex beams become much more complex. In fact, in that regime, the definition of the phase singularity is polarisation-dependent. This is what many authors have called spin-to-orbit conversion (Zhao, 2007; Vuong, 2010; Rodriguez-Herrera, 2010; Bliokh, 2010). Then, characterising vortex beams in terms of their symmetries becomes enormously useful. It allows for a systematic study of the beam without the need of considering different focusing regimes (paraxial or non-paraxial). Next, the bases to systematically characterise the symmetries under which a beam is invariant are given. Then, a general method to design structures using the spatial properties of light is sketched. Finally, two examples of the method are given. Firstly, it is shown that dielectric spheres can behave as dual materials for certain ranges of parameters. Furthermore, the role that the angular momentum of light plays in this process is unveiled. Secondly, it is shown that Whispering Gallery Modes (WGMs) can be excited on dielectric spheres without the need of evanescent coupling.

Vortex beams and symmetries

A vortex beam can be described with the following expression:

$$\overline{E}_{l,p}(\rho, \phi, z) = A_{\rho,l} \exp\left[\frac{-\rho^2}{w_0^2}\right] e^{il\phi} e^{ikz} \overline{e}_p \quad (1)$$

where (ρ, ϕ, z) are the cylindrical coordinates, $A_{\rho,l}$ is a normalisation constant, w_0 is the beam waist, l is the charge of the vortex, k is the wavenumber, and

$$\overline{e}_p = (\vec{x} + ip\vec{y})/\sqrt{2} \quad (2)$$

is a circularly polarised vector, with $p=\pm 1$, for left (+) and right (−) circular polarisations respectively. A harmonic $e^{-i\sigma t}$ is assumed throughout the remaining part of the article. The beam in Eq. (1) is a solution of the

paraxial equation (Lax, 1975). Its intensity and phase can be described with the plots on Fig. 2 for the corresponding l s. Now, the first thing that one notices is that both the intensity and phase are symmetric under translations along the z -axis. Mathematically, it means that $\overline{E}_{l,p}$ is an eigenstate of T_z the translation operator. In fact, using Noether's theorem (Noether, 1918) and group theory (Tung, 1985), it can be proven that $\overline{E}_{l,p}$ must also be an eigenstate of P_z the linear momentum along the z axis, as it is the generator of linear translations:

$$P_z[\overline{E}_{l,p}] = k \overline{E}_{l,p} \quad (3)$$

where k can be identified with the (eigen)value of P_z . Despite being less intuitive, it can also be proven that $\overline{E}_{l,p}$ is symmetric (*i.e.* it is an eigenstate) under rotations around the z axis. Now, because the angular momentum is the generator of rotations, the following relation holds:

$$J_z[\overline{E}_{l,p}] = (l+p) \overline{E}_{l,p} \quad (4)$$

With $(l+p)$ being the (eigen)value of the angular momentum. Finally, it can also be proven that $\overline{E}_{l,p}$ is symmetric under generalised duality transformations (Jackson, 1998). Then, because the helicity operator is the generator of duality transformations (Calkin, 1965), the following equation holds in the paraxial approximation:

$$\Lambda[\overline{E}_{l,p}] = p \overline{E}_{l,p} \quad (5)$$

where p is the (eigen)value of helicity. Now, there are different ways of mathematically describing non-paraxial vortex beams. One of the approaches is using the aplanatic model of a lens (Novotny, 2006) to compute the non-paraxial expression (Bliokh, 2011). Here, the symmetric properties of vortex beams will be exploited to compute their non-paraxial expression in a straight-forward manner. In order to do that, $\overline{E}_{l,p}$ are expanded as a general superposition of Bessel beams $B_{p,m,k}$. Bessel beams are a general basis of solutions of Maxwell equations. That is, any field

fulfilling Maxwell equations can be decomposed as a superposition of Bessel beams. They are also eigenstates of $P_z J_z \Lambda$, therefore, they can be used to describe E_{lp} in the paraxial approximation:

$$\vec{E}_{l,p} = \int a_k \vec{B}_{p,m,k} dk \quad (6)$$

where $m=\pm p$, and a_k are some coefficients that modulate the superposition and depend on how tightly the vortex beam is focused. The general expression of Bessel beams, as well as their paraxial approximation can be found in Fernandez-Corbaton (2012). Note that due to the fact that both E_{lp} and $B_{p,m,k}$ are eigenstates of $J_z \Lambda$, only a 1-dimensional integral has been needed. In the next sections, the symmetries of these beams will be exploited to demonstrate some effects which are unachievable with Gaussian beams (or plane waves).

Scattering control

As mentioned in the introduction, the typical approach to design nano-circuits or nano-materials is the following one. The nano-structure is characterized by its scattering matrix S . This scattering matrix is a function of many geometrical and material properties of the system, $S(g,m)$ where g and m are general sets of variables describing the geometrical and material properties of the structure. $S(g,m)$ is independent of the excitation beam. Then, the response of the structure to an incoming field E^{in} can be cast as a convolution of $S(g,m)$ with E^{in} :

$$\vec{E}^{out}(\vec{r}) = \left(S(g,m) * \vec{E}^{in} \right)(\vec{r}) \quad (7)$$

Since the properties of the structure do not depend on E^{in} and the incoming field is well-known (a Gaussian beam or a plane wave), the light-matter interaction is reduced to a complete characterization of the scattering matrix $S(g,m)$. Then, adjusting the geometry or material of the structure, a controlled interaction can be carried out. Nevertheless, this process is computationally expensive.

Symmetries can be used to get around this problem. Instead, a highly symmetric structure whose scattering matrix is well-known can be chosen as the structure. Now, given this limitation, the sought interaction can be obtained by modifying the plane wave content of the excitation beam in a controlled manner. That is, instead of controlling E^{out} with the geometry and materials of the structure, the interaction is controlled with the incoming field E^{in} :

$$\vec{E}^{out}(\vec{r}) = \int d^3 k_i \exp(i\vec{k}_i \cdot \vec{r}) \left(S(g,m) * \vec{E}^{in}(\vec{k}_i) \right)(\vec{r}) \quad (8)$$

where \vec{k}_i are each of the different plane waves that take part in the superposition, and $E^{in}(\vec{k}_i)$ is the Fourier transform of the incident field, which modulates the plane wave decomposition. Symmetries play a double role here. First, they simplify the scattering matrix of the structure. Second, they bind the values that E^{out} can take. That is, when the symmetries of E^{in} are matched with the symmetries of the sample, then E^{out} must preserve the symmetries of E^{in} . For example, if the sample is cylindrically symmetric and E^{in} is a Bessel mode $B_{p,m,k}$, then E^{out} will have the same J_z value:

$$\vec{E}^{out}(\vec{r}) = \int dk \left(a_{k',p} \vec{B}_{p,m,k'} + a_{k',-p} \vec{B}_{-p,m,k'} \right) \quad (9)$$

but in principle the helicity value p could change and also new k components could be created. Next, two applications of this conceptual method are given. First, it is shown that a non-dual material can be turned effectively into a dual one if the proper vortex beam is chosen as illumination. Secondly, it is seen that vortex beams can excite WGMs, without the need of any evanescent coupling.

Inducing dual behaviour

A dual material can be defined as a material that preserves helicity upon scattering (Fernandez-Corbaton, 2013a; Zambrana-Puyalto, 2013c). The definition stems from the fact that helicity is the generator of

generalized duality transformations. Recently, it has been proven that such a macroscopical material can only exist if the electric permittivity and magnetic permeability of all its subparts have a constant ratio (Fernandez-Corbaton, 2013a):

$$\frac{\epsilon_i}{\mu_i} = \text{const.} \quad (10)$$

Interestingly, the microscopic Maxwell equations are not symmetric under duality transformations, as there are no magnetic monopoles in the universe. However, in the macroscopic approximation, Eq. (10) is enough to grant the material with a dual behaviour. Dual materials are useful for many different applications. They can be used to reduce the backscattering of samples (Fernandez-Corbaton, 2013a; Zambrana-Puyalto, 2013b), to create perfect optical rotators (Fernandez-Corbaton, 2013b), or to scatter light without changing the polarisation (Fernandez-Corbaton, 2013a), among others. Nevertheless, Eq. (10) is still very restrictive, and some other approximations can be done.

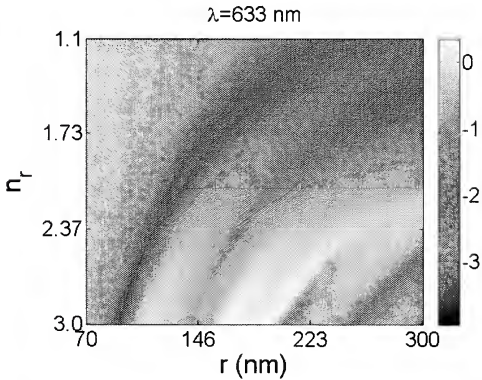


Figure 3: Plot of $\log|T_p(r, n_r)|$ as a function of r and n_r . The purple curve indicates the combination of parameters for which the sphere is dual. The incident field is a Gaussian beam with a wavelength of $\lambda = 633\text{nm}$.

It was analytically proven in Zambrana-Puyalto (2013c) that if certain combinations of $\{r, \lambda, n_r\}$ are used, non-dual dielectric

dipolar particles can behave as dual under a Gaussian excitation. r is the radius of the sphere, λ is the wavelength of the excitation, and n_r is the relative refractive index of the particle with respect to the medium surrounding it. This phenomenon is summarised in Fig. 3. A Gaussian beam excites a sphere at $\lambda = 633\text{nm}$ and the scattering is split into its two helicity components. Then, the component with the same helicity as the incident light is divided over the opposite one. This defines an adimensional transfer function $T_p(r, n_r)$, and its logarithm is depicted in Fig. 3. When $\log|T_p(r, n_r)| \rightarrow -\infty$, then the sphere behaves as dual. As it can be seen in the horizontal axis of Fig. 3, the sphere is indeed dipolar (its size is much smaller than the wavelength). In fact, the same results have been experimentally demonstrated very recently by Geffrin (2012), Fu (2013) and Person (2013).

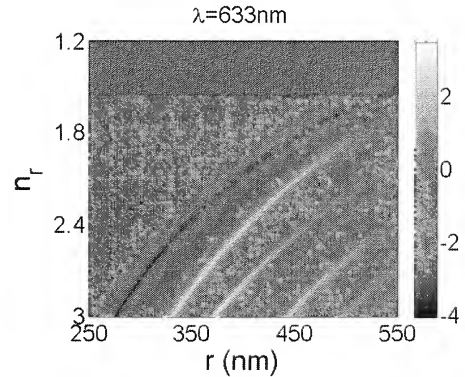


Figure 4: Plot of $\log|T_p(r, n_r)|$ as a function of r and n_r . The incident field is a vortex beam $E_{l=4, p=1}$ at $\lambda = 633\text{nm}$. Again, the purple curves indicate the parameters for which the sphere is dual. Note that the size of the sphere is not dipolar in this case, as r varies from 250 to 550nm.

Now, vortex beams can be used to extend this behaviour to particles of any size. The idea is that even though the particle gets bigger, the scattering of the first multipolar

orders can be cancelled by choosing the corresponding vortex beam. In Fig. 4, a vortex beam $E_{l=4,p=1}$ is used, and as a consequence particle of almost $1\mu\text{m}$ of size can behave as dual. Clearly, the choice of a vortex beam simplifies the problem. It would be much more complex to design a metamaterial of that size with similar features.

Excitation of Whispering Gallery Modes

Whispering Gallery Modes (WGMs) are widely used in physics. Their incredibly high Q factors make them perform very well to probe any sort of disturbance in the environment (Schiller, 1991; Oraevsky, 2002; Vahala, 2003). Also, they can be used in quantum information processes, such as quantum optomechanics (Lee, 2010; Forstner, 2012). In Oraevsky (2002), it is demonstrated that a plane wave cannot excite a WGM. Instead, an evanescent wave must be used to excite one of these modes. WGMs are actually modes of light with very large value of J_z , of the order of 1000 occasionally (Schiller, 1991; Oraevsky, 2002). An alternative way of exciting WGMs without the need of using fibers or prism to create evanescent waves is sketched here. It is based on the fact that spheres are symmetric under rotations around the z axis. Thus, if a sphere is excited with a vortex beam with a large value of J_z , the scattered field must preserve that large number of J_z (Zambrana-Puyalto, 2012; Zambrana-Puyalto, 2013a). However, the incident beam must fulfil another condition in order to excite a WGM with a high Q factor. The Q factor of the mode drastically depends on the coupling between the incident beam and the sphere. This coupling is modelled by the so-called Mie coefficients (Bohren, 1983). In order to ensure a good overlap between the incident vortex beam and the WGM, the following condition between $\{r, \lambda, n_r\}$ needs to be

fulfilled (Zambrana-Puyalto, 2012; Zambrana-Puyalto, 2013c):

$$r \approx \frac{m\lambda f(n_r)}{2\pi} \quad (11)$$

where m is the value of J_z of the WGM, and $f(n_r)$ is a function of the relative refractive index that can be calculated (Zambrana-Puyalto, 2013c). When both conditions are fulfilled, a high-Q WGM can be excited with a vortex beam, without the need of carrying out any evanescent coupling.

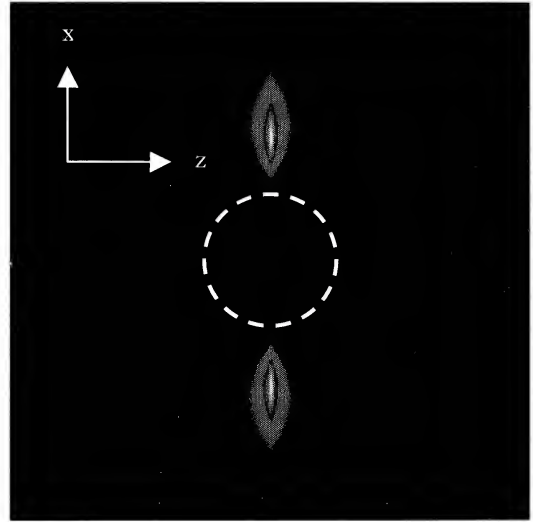


Figure 5: Intensity plot of a scattered WGM of order $m=15$. Yellow means maximum intensity, and black minimum. The dashed circle depicts the position of the sphere. In order to obtain such a scattered field, an incident vortex beam $E_{l=14,p=1}$ propagating in the z axis has been used. The excitation is at $\lambda=633\text{nm}$, and the particle is made of a material such that $n_r=1.5$, which implies that $f(n_r)=0.8$ (Zambrana-Puyalto, 2013c). Its radius is $r=1.2\mu\text{m}$.

Conclusions

It has been shown that the symmetries of light can be used to control the scattering of nano-structures. In particular, vortex beams, which can be symmetric under rotations, translations, and duality transformations, have

been used to control two scattering events. Firstly, they have been used to induce duality symmetry in an arbitrary large dielectric non-dual sphere. And secondly, they have been used to excite WGMs without the need of using evanescent couplings.

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Past and Present Challenges in Catalysis: Developing Green and Sustainable Processes

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Abstract

This article is based on a lecture by one of the four recipients of the Royal Society of New South Wales Scholarships for 2013, delivered at the Union, University and Schools Club, on Wednesday, 5 February 2014. It briefly discusses the role of societal, political, and environmental drivers on the development of catalysts in the 20th century, which led to the technological advances that enabled the modern lifestyle we enjoy today. Three challenges of catalysis in the 21st century will then be discussed in more detail, with a focus on changing feedstocks from fossil resources to biomass resources, and the growing emphasis on lower energy, 'greener' processing.

Keywords: Catalysis, biomass, green chemistry, sustainability.

Introduction

Catalysts play a central role in chemistry, and are used in approximately 90% of all industrial chemical processes (Thomas and Williams 2005, Armor 2011, Thomas 1994). In the last 250 years, especially during the 20th century, catalysts were involved in many technological developments that contributed to the lifestyle and standard of living that we enjoy today. Many of these developments emerged due to the convenience and abundance of fossil feedstocks. However, with global energy demands expected to double within the next forty years, peak oil being reached soon or even past, the growing concerns surrounding carbon dioxide emissions, and the political instability related to geographical restrictions of oil reserves, there is a growing need for greener processing and to develop alternative resources. Just as

catalysts played an important role in the 20th century, they are expected to have an ever more crucial role in the 21st century, as will be discussed in the subsequent sections.

Historical Perspective

The first use of catalysts can be traced back approximately 10 000 years, with depictions of brewing on archaeological remains (Adams 2009). Even back then, catalysts had an important role for humankind! However, it was not until the 19th century that the concept of catalysis was understood. Jöns Jacob Berzelius introduced the term *catalysis* in 1835 before Wilhelm Ostwald provided a scientific definition in 1895 (Zaera 2012). Over the next century, catalysts played a significant role in the development of industrial processes that have greatly influenced modern society. Arguably the most important catalytic

development was the Haber–Bosch process, which is promoted by iron-based catalysts. Motivated by the need for fertiliser during the anticipated Chilean embargo on saltpetre, this process has had an enormous impact on the development of modern society. On the one hand, it was responsible for between 100 and 150 million deaths in the 20th century because of its role in the production of explosives and chemical weapons used in armed conflicts (Erisman et al. 2008). Indeed, the demand for explosives based upon nitric acid had a huge impact on the growth of the industrial production of bulk chemicals during World War One (Lindstroem and Pettersson 2003). On the other hand, the Haber–Bosch process is responsible, through the production of agricultural fertiliser, for feeding approximately 48% of the world's population in 2008 (Fig. 1) (Erisman et al. 2008). As will be shown briefly in this section, major catalytic developments rarely occurred in isolation. Rather, they required societal, political, or environmental motivations as drivers. Equally important was the accessibility to raw materials, and in turn, new technology created new demands.

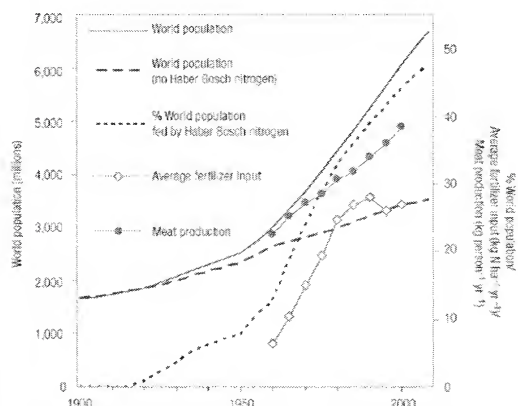


Figure 1: Trends in human population and nitrogen use in the 20th century. Reprinted by permission from Macmillan Publishers Ltd: NATURE GEOSCIENCE. Erisman et al. *Nature Geoscience*, 1, 10 (2008), copyright 2008.

Although the first crude oil was drilled in 1859, the main feedstock for chemicals at the onset of the 20th century was coal, based mainly on coal liquefaction, distillation of coal tar, acetylene, and coal gasification (Armor 2011). As the demands for explosives diminished, the focus after World War One moved to synthetic fuels. Among the most important catalytic developments in this period was the use of iron and copper catalysts for the synthesis of hydrocarbons from carbon monoxide and hydrogen (obtained from coal) by Franz Fischer and Hans Tropsch in 1923. The Fisher–Tropsch synthesis of fuels is just as relevant today as it was nearly a century ago. Nonetheless, the widespread use of crude oil as a feedstock began when Eugène Houdry developed the catalytic cracking of petroleum in 1936. Lewis and Gillian modified the process with the introduction of fluid catalytic cracking (FCC) in 1941, and this improvement enabled the supply of the vast quantities of high-octane aviation fuel needed to supply the Allied Forces in World War Two.

With the end of the war, needs again changed with society, and the automobile market accelerated in Europe. The increased demands for gasoline created the petrochemical industry, as petroleum refining enabled the production of plastics, pharmaceuticals, and specialty chemicals. Crude oil became entrenched as a convenient and accessible feedstock. The most important development during this period was the use of a modified X zeolite catalyst in the FCC of petroleum, and one of the most important concepts in zeolite catalysis was the discovery of shape-selective catalysis in zeolites (Masters and Maschmeyer 2011). With these advances, zeolites revolutionised the catalytic cracking and hydrocracking of the crude oil feedstocks, dramatically improving yield and process efficiencies.

Indeed, the use of zeolite catalysts is estimated to save the petroleum industry 10 billion dollars a year (Weitkamp 2000).

As the transportation industry and chemical processes expanded, research into new catalysts was required to meet the regulations regarding vehicle and stationary engine emissions. Hydrodesulfurisation was developed in the 1960s for the removal of sulfur in fuels. In 1974, the first oxidation catalytic converter for automobiles was developed, followed by the three-way catalytic converter in 1978, and the Pd three-way converter in the 1990s. By 1990, the catalytic converter had reduced emissions from hydrocarbons, NO_x, and CO from vehicles by 90% compared to levels in 1965 (Armor 2011).

Although emissions control catalysts are among the exceptions, the fundamental studies on catalysts in the 20th century were mostly focused on achieving high turnover rates. There is now a growing need to develop alternative resources and lower energy, 'greener' processing. Catalysts are expected to play a huge role as many of the challenges of the previous century will be revisited with changing feedstocks, as will be discussed in the subsequent sections.

Catalysts in the 21st Century

The Need for Green and Sustainable Processes

The U.S. Energy Information Administration anticipates that worldwide energy use will grow by 56% between 2010 and 2040, which is equivalent to global energy demand increasing by approximately 1.5% a year (EIA 2013). More than 85% of this increase occurs due to the strong economic growth and expanding populations in developing nations. However, this rapid increase in energy

demand is problematic as finite fossil resources (coal, oil and gas) currently provide 85% of the world's energy (IPCC 2011). Of the three, oil is the most concerning, as worldwide reserves of oil are sufficient for only another 55 years (IEA 2012). Indeed, a recent article in *Nature* argues that 'peak oil' (the time when global production of oil reaches a peak before declining) was passed in around 2005 (Murray and King 2012). Access to the worldwide oil reserves is also compromised due to political instability (*e.g.* in the Middle East, an area which accounts for almost 50% of proven oil reserves at the end of 2012) (BP 2013), causing problems of energy security to developed countries. Moreover, the level of carbon dioxide in the atmosphere has increased by approximately 40% compared to pre-industrial levels, largely because of the surge in fossil fuel consumption and land use changes (Edenhofer et al. 2012). This increased carbon dioxide has serious consequences for global warming, with the International Panel on Climate Change affirming human influence as "extremely likely" (*i.e.* 95–100% probability) to be the dominant cause of climate change (IPCC 2013).

Green Chemistry and Catalysis

The last thirty years has seen a significant move towards green chemistry, as it is recognised that the challenges of sustainability will be met with new technologies that provide society with energy and materials in an environmentally responsible manner (Anastas and Kirchhoff 2002). The Brundtland commission defined sustainable development in 1987 as "Meeting the needs of the present generation without compromising the ability of future generations to meet their own needs" (Brundtland 1987). Four years later, Anastas defined green chemistry as "the utilisation of a set of principles that reduces or eliminates

the use or generation of hazardous substances in the design, manufacture and application of chemical products” (Anastas and Warner 1998). These Twelve Principles of Green Chemistry, listed in Figure 2, are the means to achieving sustainable development.

The Twelve Principles of Green Chemistry	
1.	It is better to prevent waste than to treat or clean up waste after it is formed.
2.	Synthetic methods should be designed to maximize the incorporation of all the materials used in the process into the final product.
3.	Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4.	Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5.	The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible, and innocuous when used.
6.	Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7.	A raw material or feedstock should be renewable rather than depleting wherever technically and economically practicable.
8.	Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9.	Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10.	Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11.	Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12.	Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Figure 2: *The Twelve Principles of Green Chemistry*
(Anastas and Warner 1998).

The Twelve Principles comprise of three main aspects, identified by Sheldon. The first aspect aims to minimise waste through the efficient utilisation of raw materials (Sheldon 2014). Waste is defined as any material that is generated in a process that does not have realised value and includes the loss of unutilised energy (Anastas and Eghbali 2010). With the need to double energy production

within the next forty years (without increasing carbon dioxide emissions), the need to develop more energy efficient processes is essential. Secondly, avoiding the use of toxic and/or hazardous substances is important to circumvent health, safety and environmental issues. This aspect includes avoiding the use of solvents, which often account for the majority of mass wasted in syntheses and processes (Anastas and Beach 2007). Finally, the third aspect identified by Sheldon is the use of renewable biomass feedstocks instead of non-renewable fossil feedstocks. Biomass conversion has become an important area of research due to the need for new technologies to obtain energy and chemical feedstocks in a sustainable manner (Huber et al. 2006, Corma et al. 2007), and it is a major aim of green chemistry (Anastas and Beach 2007).

The motivations and drivers in the 21st century have changed. With the need for alternative resources, catalysts are expected to play an ever more crucial role in the technological developments for biomass conversion, enabling pathways previously unavailable in processing alternative feedstocks. Catalysts are also fundamental to improving the efficiency of reactions by lowering energy input, by avoiding the need for stoichiometric quantities of reagents, by decreasing the use of processing and separation agents, and by offering greater product selectivity (Anastas and Eghbali 2010, Anastas et al. 2001). Over the next few decades, catalytic processes will be developed to convert biomass to fuels and chemicals, but no developments will be made that are not informed by the thinking of green chemistry and that do not fulfil their role in a sustainable manner.

Current Challenges in Catalysis

For the remainder of this paper, three different but related novel applications of

catalysis to address the challenges of the 21st century will be discussed. This paper will focus on biomass as a renewable feedstock for fuels and chemicals, and the move towards lower energy, 'greener' processing. It is by no means a comprehensive investigation of all the challenges facing catalysis, but comprises of three niche areas of particular interest to the author. A brief context will be given highlighting the current challenges in each area, and an example of how these problems can be met based on the PhD research of the author will be provided.

Designing Sulfur Resistant Catalysts for Biomass Processing

With oil supplies diminishing significantly over the next few decades, there is an increasing need to develop liquid transport fuels from biomass. Due to the chemical, thermal and functionality differences between biomass and petroleum feedstocks, new chemical pathways need to be developed for biomass processing (Demirbas 2007, Huber and Dumesic 2006). The current technologies for the conversion of biomass include gasification, pyrolysis, hydrothermal liquefaction, delignification followed by saccharification and fermentation, and aqueous phase reforming (APR). Many of these processes involve catalysts, such as APR, which is a promising technology that uses supported metal catalysts to convert biomass-derived feedstocks into either hydrogen or alkanes (Cortright et al. 2002, Chheda et al. 2007).

An important challenge in developing catalysts for biomass conversion, including APR, is operating the catalysts in the presence of sulfur in real biomass feedstocks (e.g., wood: approx. 56 ppm), due to the presence of sulfur-containing amino acids and from the uptake of nutrients in the soil (Robinson et al. 2009). This sulfur is a problem because sulfur

is known to poison noble metal catalysts (Bartholomew et al. 1982, Rodriguez 2006). (Bartholomew et al. 1982, Rodriguez 2006) Although the sulfur tolerance of catalysts was widely investigated in the 20th century, both for the petrochemical and fine chemical industries (Bartholomew et al. 1982, Rodriguez and Goodman 1991, Somorjai 1994), there has been little research into improving the sulfur resistance of catalysts for use with biomass feedstocks. Thus, developing sulfur resistant catalysts for biomass processing is one of the catalytic challenges of the 20th century that is being revisited in the 21st century as feedstocks change from fossil resources to biomass resources.

We have recently designed supported bimetallic Pt-Ru catalysts that exhibit improved sulfur resistance and show promising potential for APR of model compounds, using the hydrogenation of cyclohexane as a screening reaction (Stanley et al. 2011). Thiophene was used as the model sulfur source. In all cases, the bimetallic catalysts achieved higher turnover frequencies than their monometallic counterparts in both the absence and presence of the sulfur-containing species. Indeed, the bimetallic catalysts remained active even in reactions having *ten times* the concentration of sulfur expected in woody biomass feedstocks, suggesting the operation of a sulfur/hydrogen spillover equilibrium. In contrast, the monometallic catalysts were completely poisoned.

Powder X-ray diffraction (XRD) and extended X-ray absorption fine structure (EXAFS) experiments were used to probe changes to the Pt unit cell and Pt/Ru bonding environments induced by sulfur poisoning for the bimetallic catalysts (Stanley et al. 2011, Stanley et al. 2014). The results

from these investigations are consistent with increasing concentrations of sulfur-containing species coordinating to the ruthenium atoms during sulfur poisoning, leading to a partial separation of the alloy. However, after regenerating the poisoned catalysts under pure hydrogen to remove the sulfur species, the alloy is reformed, showing that this process is reversible. Thus, these results are consistent with an *in-situ* self-regeneration mechanism, which we propose is occurring to enable the bimetallic catalysts to remain active. That is, during poisoning the catalyst partially dealloys, but a sulfur spillover and a hydrogen spillover take place to regenerate the catalyst *in-situ*, and the metals are then re-alloyed. The catalysts are sulfur-resistant.

Hydrogenation of Aromatics and Hydrogen Storage

The second catalytic challenge facing the 21st century fits in with the drive towards lower energy, 'greener' processing. In the previous century, the focus of fundamental studies was largely on achieving high turnover rates. Now, the main drivers for technological developments have changed, and a greater focus is on reducing energy requirements. The hydrogenation of aromatics is an important reaction both for small-scale synthesis and for industrial reactions, including the production of cyclohexane, which is an important precursor for the manufacturing of nylon-6,6 (Mevellec et al. 2006, Park et al. 2005, Roucoux et al. 2003). These reactions are traditionally carried out using elevated temperatures and pressures, which often exceed 100 °C and 50 atm H₂ (Augustine 1995). Furthermore, aromatic compounds are responsible for undesired particle emissions in exhaust gas, leading to a tightening of fuel legislation (Stanislaus and Cooper 1994, Cooper and Donnis 1996). Thus, being able to perform the hydrogenations under mild conditions is an

important challenge in terms of energy efficiency and environmental concerns.

Additionally, the reversible toluene/methylcyclohexane couple has the added interest of being a safe and feasible hydrocarbon combination for the storage of hydrogen (Alhumaidan et al. 2011). Cyclic hydrocarbons have a relatively high hydrogen storage capacity, produce no carbon dioxide or carcinogenic products, and their volatility range makes them compatible with existing infrastructure such as refuelling stations and oil tankers for the storage and transportation of the liquid hydrocarbons (Kariya et al. 2002, Kariya et al. 2003, Hodoshima and Saito 2009, Alhumaidan et al. 2011). Thus, the cyclic hydrocarbon combinations have a distinct advantage over other solid hydrocarbons for hydrogen storage.

Over the last ten years, there has been an increased focus on effecting the hydrogenation of toluene under mild conditions, particularly at room temperature. However, the catalyst preparations are often challenging, and the resulting catalysts often have poor activity and/or poor stability (Park et al. 2005). Several groups have demonstrated that metal nanoparticles can perform the reactions with highly water-soluble surfactants used to stabilise these particles in aqueous solution (Schulz et al. 2002, Schulz et al. 1999, Schulz et al. 2000, Fonseca et al. 2003, Mevellec et al. 2004, Hubert et al. 2009a, Hubert et al. 2009b, Roucoux et al. 2003), while others have investigated the use of ionic liquids for nanoparticle stabilisation (Fonseca et al. 2003, Scheeren et al. 2003, Silveira et al. 2004, Rossi and Machado 2009). Further still, a range of solid supports has been used in an attempt to overcome the problems of stability (Bianchini et al. 2003, Park et al. 2005, Mevellec et al. 2006, Park et al. 2007b, Park et al. 2007a,

Takasaki et al. 2007, Barthe et al. 2009a, Barthe et al. 2009b, Pan and Wai 2009, Péliesson et al. 2012, Song et al. 2009, Zhou et al. 2009, Jahjah et al. 2010, Fang et al. 2011, Hubert et al. 2011, Zahmakiran et al. 2010). However, in many cases the reaction and/or catalyst manipulations required air-free conditions and, where special precautions were not required, elevated hydrogen pressures were again used.

To overcome these challenges, we have developed robust bimetallic supported Pt-Ru catalysts that, remarkably, operate under one atmosphere to rapidly catalyse the room temperature hydrogenation of toluene (and tetralin) at 1 atm H₂ (Stanley et al. 2013a). Higher turnover frequencies were achieved with the bimetallic catalysts compared to their monometallic counterparts, suggesting a synergistic effect between platinum and ruthenium. These easily handled, air-stable catalysts are amongst the most active catalysts for aromatic hydrogenations under ambient conditions reported to date.

Green Catalytic Processing of Lignin

Returning to renewable feedstocks, the third challenge is the need to develop the catalytic technologies to obtain chemicals from alternative resources. As already mentioned, biomass is the only renewable source for carbon-based materials. Lignin (which constitutes approx. 15–30% by weight and 40% by energy content of lignocellulosic biomass (Perlack et al. 2005)) is particularly valuable, as its unique structure as an amorphous, highly substituted, aromatic polymer makes it the major renewable source of aromatics (Zakzeski et al. 2010). However, synthetic approaches for the conversion of lignin to chemicals are markedly less developed compared to the cellulosic components of biomass, partly due to the recalcitrant nature of lignin that provides

plants with their strength (Zakzeski et al. 2012). Much effort is currently being devoted to the development of new technology to process low value lignin into higher value-added chemicals. Although aggressive depolymerisation of lignin yields chemicals such as benzene, toluene, and xylene, as well as phenols and aliphatic hydrocarbons used in conventional chemical processes, the selective depolymerisation of lignin could yield monomeric lignin aromatics which are not accessible by traditional petrochemical routes. For example, these monomeric lignin aromatics could be obtained from the pretreatment streams of the pulp and paper industries, which alone produced 50 million tons of extracted lignin in 2004 (Zakzeski et al. 2010). Extraordinarily, the vast majority of this type of lignin is burned as a low value fuel – only 2% is used commercially (Gosselink et al. 2004).

Now, analogous to the petroleum refinery, a biorefinery could use biomass feedstocks to produce a range of products. As outlined earlier, the petroleum refinery developed over many decades in the 20th century, as crude oil emerged as a convenient and readily available feedstock. It began with only few products, but as the needs changed with those of society and new catalytic technology was developed, it expanded to produce plastics, pharmaceuticals, and speciality chemicals. With the growing need to obtain these products from renewable resources, the biorefinery is emerging. In the early stages, the biorefinery will need to produce large volumes of more chemically accessible, lower value fuels. Later, higher value chemicals produced in smaller quantities will be required to offset the costs (Bozell and Petersen 2010). Finally, it is expected that all components of biomass will need to be used for a biorefinery to be economically viable. Catalysts are critical to the development of the new

technology for enabling the conversion of biomass. The catalytic challenges for performing the chemical transformations, which were overcome for crude oil over many decades in the 20th century in the petroleum refinery, are being revisited with biomass-derived feedstocks in the 21st century in the biorefinery.

Currently, there are two approaches for converting biomass-derived resources into higher-value added fuels. The first is a drop-in strategy, where the biomass feedstocks are transformed into existing platform chemicals, to directly replace well-established chemicals currently produced from fossil feedstocks (Vennestrom et al. 2011, Dapsens et al. 2012). The other approach, which we favour, is a curiosity driven broad-based strategy that exploits the existing structure and functionality of biomass. In this approach, renewable platform chemicals based on the structure of biomass could lead to the development of new chemistry and, in the longer term, a plethora of chemical products with as yet unknown applications (Zakzeski et al. 2010).

Fundamental to establishing the required catalytic technology for converting biomass-derived feedstocks into chemicals is an understanding of the reactivity trends and reaction pathways. It has been recognised that many of the building blocks obtained from the disruption of lignin into monomeric aromatics resemble *p*-coumaryl, coniferyl, and sinapyl alcohol. We have recently shown that model compounds based on the *p*-coumaryl structure, specifically cinnamyl alcohol and 4-(3-hydroxypropyl)phenol, can be selectively transformed into different products by catalytic methodologies based on dimethyl carbonate (DMC) as a green solvent/reagent (Stanley et al. 2013b). This selectivity can be tuned by varying the reaction temperature

and the nature of the catalyst. In general, basic catalysts promote selective transesterification of the aliphatic hydroxyl group at 90 °C. On the other hand, amphoteric solids such as alkali metal-exchanged faujasites selectively produce the corresponding alkyl ethers at higher temperatures (165–180 °C). Phenolic hydroxyl groups can be similarly methylated with the faujasites at high temperatures. Thus, these results indicate that efficient and selective catalytic upgrading of lignin-derived chemical building blocks is possible with DMC, and the preliminary screening for selectivity illustrates the reactivity trends and the most promising synthetic pathways.

Conclusions

Catalysts will play a crucial role in the 21st century in moving away from fossil resources. Although oil will still be the main source of fuels and chemicals in the earlier part of this century, there is a great need to improve our current processes to make them more energy efficient. The development of robust catalysts that perform reactions at lower temperatures and pressures is one way to achieve this aim. However, biomass is the only sustainable source of liquid transportation fuels and aromatic chemicals, and the development of new catalytic technology and chemical pathways for use in the biorefinery is essential. Nonetheless, there is no one solution to addressing the challenges of sustainable development. The 21st century will require a combination of solar, geothermal, wind, biomass, hydrogen, and nuclear to meet our energy needs.

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An overview of biosimilars

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Abstract

Biologics have become an increasingly important but also expensive part of the global medicinal cabinet. Generics of this class of drug, termed biosimilars, can relieve the financial burden on healthcare systems and improve patient accessibility. This mini-review covers the evolving international regulatory legislation for biosimilars, challenges for biosimilar development and expected developments.

Keywords

Biosimilars, biologics, regulatory guidelines, safety

Introduction

Biopharmaceuticals or biologics have revolutionised medicine, advancing the treatment of diseases from rheumatoid arthritis to cancers. Over the last decade, they have experienced an explosive growth and now account for an astounding 30% of global pharmaceutical research and development spending (McCamish et al. 2012). In 2012, five of the top 10 global best-selling prescription drugs were biologics (Lindsley 2013), and sales of this class of medication are expected to reach USD 150 billion worldwide by 2015 (Butler et al. 2012). In turn, biologics are expensive and expend enormous portions of government healthcare budgets. For example, in the US, 50% of the charges for the top 20 drugs in outpatient oncology clinics are for biologics (Hirsch et al. 2013).

‘Generic’ biologics, defined as a copy of an existing approved biologic with demonstrated similarity in physicochemical characteristics, efficacy and safety (Weise et al. 2011), are therefore much sought after to relieve healthcare costs and increase access to treatment (Roger 2010).

Generics of small molecule drugs enter the market rapidly after patent expiry of the original pharmaceutical, leading to robust competition and significant cost reductions to patients. However, unlike small molecule drugs, the development of ‘generic’ biologics is not straightforward. Biologics are a pharmaceutical drug class that is defined by their production in living systems, such as bacteria or mammalian cells. The majority of biologics are proteins and thus entail a

complex manufacturing process. The primary steps involve the cloning of the relevant gene into a complementary DNA (cDNA) vector, which is then transferred into a host cell (typically from *Escherichia coli*, yeast or Chinese Hamster ovary cells) (Dranitsaris et al. 2011). An optimal cell-line is chosen, then expanded and purified into the bulk drug for validation and quality control processes (Papp et al. 2013). These manufacturing techniques and cell lines are typically proprietary, and the complexity of these molecules makes development of ‘generic’ biologics significantly more expensive than for small molecules (Casadevall et al. 2013).

Additionally, the large number of process variables, lack of access to the original cell line and the sensitivity of biologics to manufacturing conditions, means that ‘generic’ biologics are unlikely to completely replicate the reference product. Thus ‘generics’ of biologic drugs are appropriately termed biosimilars, as they are likely to contain some structural or functional differences (Kanter et al. 2012, Ebbers et al. 2012). Whilst these molecular differences may not be detectable with existing technology, they can have potentially important impacts on the safety and efficacy of the drug (Papp et al. 2013). Thus the definition of a biosimilar is further defined as being highly similar to the innovator product, notwithstanding minor differences in clinically inactive components (Konski 2011). Whilst the standard approach for generic small molecule drugs consists of comparative bioavailability studies, these are inadequate for bringing a biosimilar to market. Rather, comprehensive comparability analyses with the reference biologic are generally required, which contribute to the cost of development (Weise et al. 2011).

The first biosimilars became available with the “Guideline on similar biological

medicines”, which was introduced in the European Union (EU) in 2005 (Dalgaard et al. 2013). Whilst a number of biosimilars have since become available, including 14 in the EU (Dranitsaris et al. 2011), their market penetration has been relatively slow. For example, in Denmark, biosimilars of Filgrastim have gained less than 10% of the market (Hirsch et al. 2013). However, an unprecedented opportunity for rapid growth of the biosimilars market is fast approaching, with 12 patents for biologics expiring before 2020 (Pani et al. 2013). Indeed, the worldwide market for biosimilars is expected to grow to USD 3.7 billion by 2015, from just USD 243 million in 2010 (Konski 2011). The future potential for biosimilars is even greater, with more than 100 original biologics in current clinical use and many more under development (Roger 2010).

Nonetheless, biosimilars continue to face regulatory and commercial uncertainties, which are discussed below.

Current legislation and regulatory guidelines

Clear regulatory guidelines for biosimilars are essential for both manufacturer investment and acceptance by clinicians and patients. In general, international regulatory bodies agree that standards for approval of biosimilars differ from those for small molecule generics, and typically emphasise the need for direct analytical and biological comparison to the reference biologic (Papp et al. 2013). Additionally, rigorous post-approval pharmacovigilance programs are mandated to rapidly identify any serious adverse effects (Dranitsaris et al. 2011). Nonetheless, the requirements are less than for a new biologic and an abbreviated approval pathway is defined, though at the current time of writing, there is no single uniform international

guideline for biosimilars. Rather, there is a dichotomy of a highly regulated and a less regulated registration pathway. Existing global regulations have been extensively reviewed by Konski et al. (2011) and Dranitsaris et al. (2011).

Highly regulated approval pathways

European Medicine Agency (EMA)

Since the release of the initial “Guideline on similar biological medicines” in 2005, the EMA has continued to be at the forefront of legislation governing biosimilars and a standard for regulatory authorities in other countries. Current guidelines are well-defined, and address major concerns including safety, immunogenicity, clinical efficacy and the extrapolation of indications. Additionally, the material is tailored to specific classes of biosimilar agents, such as erythropoietin, insulin, growth hormone, low molecular weight heparin and interferon alpha (Dranitsaris et al. 2011). This is necessary as the complex characteristics of biologic molecules means that a ‘one size fits all’ assessment of biosimilarity is inadequate (Kozlowski et al. 2011). Interestingly, the EU guidelines do not discuss the issue of interchangeability or automatic substitution of biosimilars for the original drug as this is decided by individual EU nations. (Weise, 2011).

A criticism of the EMA position on biosimilars is its emphasis on clinical proof of similarity, which has been a deterrent to some biosimilars applicants. Following significant improvements to analytical characterization techniques over recent years, the EMA has indicated that it may begin to increase reliance on analytical data (Senior 2013). Kozlowski et al. (2011) commented that clinical requirements may eventually be reduced as analytical techniques eventually will allow for extensive use of “fingerprint” comparison

between a biologic and biosimilar. This resulting cost-savings of biosimilar development might then be passed on to the patient. However, animal and clinical studies will still be required in the near future to provide adequate early safety and efficacy data (Kay 2011).

US Food and Drug Administration (FDA)

In 2009, US congress passed the Biologics Price Competition and Innovation Act (BPCIA) as part of Patient Protection and Affordable Care Act, which empowered the FDA to identify an abbreviated approval pathway for biosimilars (Kozlowski et al. 2011). Prior to this, the FDA already had indirect experience evaluating biologics and biosimilars (McCamish et al. 2012). Firstly, new drug applications for biologics via the FD&C Act whereby biosimilars could follow an approval pathway similar to that of small molecules. Secondly, via comparability testing that are enforced when any manufacturing process changes are made for original biologics (e.g. scale-up and modernizing the process). Given this prior knowledge and the detailed European experience and guidelines, the US approach to the approval process for biosimilars can be greatly accelerated. However, it appears from previous meetings with stakeholders, that the FDA is unlikely to directly adopt the EMA guidelines (Dranitsaris et al. 2011).

In 2012, the FDA issued draft guidance documents that included scientific and regulatory considerations for biosimilar applicants (Papp et al. 2013; Casadevall et al. 2013). Interestingly, the FDA guidelines provision for the interchangeability or automatic substitution of biosimilars (Weise, 2011). However, unlike small molecule drugs, frequent interchanging of biologics can compromise the safety and efficacy of the

medication, potentially leading to severe immune reactions. The FDA has yet to determine the data necessary for such a designation, and only experience over time will determine the extent and validity of biosimilar interchangeability (Kay 2011), Kozlowski et al. 2011).

Other countries

A number of other countries have followed the highly regulated pathway, with requirements based on the EMA guidelines.

The Canadian food and drug regulatory agency (Health Canada) has termed biosimilars as ‘subsequent entry biologics’, which are treated as a new drug submission. Direct substitution or interchangeability is not permitted and guidance is for specific drug classes only (Papp et al. 2013, Dranitsaris et al. 2011). At this time, only a single biosimilar (Omnitrope, containing the human growth hormone somatropin) has been approved (Papp et al. 2013). The Canadian guidelines are discussed in detail by Papp et al. (2013).

The Australian Therapeutic Goods Administration (TGA) has also adopted the European guidelines for approval of biosimilars. Because biosimilars will be assessed on a case-by-case basis, a pre-submission meeting with the TGA is encouraged for manufacturers to determine data requirements. Omnitrope has been approved for use in Australia since 2006 (Roger 2010, Dranitsaris et al. 2011).

Less regulated regulatory pathways

In some countries, approval criteria for copies of original biologics are less stringent to accelerate their potential for cost savings. For coherence of the manuscript we describe these as biosimilars. However, the less rigorous comparative assessments in these countries have seen them referred to as a

‘biopharmaceutical not subjected to regulatory approval’ (Roger 2010). Nonetheless, in China and India, this approach has resulted in a wide range of these less regulated biosimilars being available or under development (Dranitsaris et al. 2011). However, the guidelines for them are relatively vague.

China

China’s biosimilar law, which is regulated by State Food and Drug Administration (SFDA), states that a biosimilar product must be registered and approved as a new biological product. This is regardless of whether the originator drug is commercially available in the Chinese market. Whilst a biosimilar may be given an abbreviated approval process, this appears to be implemented and defined at the discretion of the SFDA (Konski 2011).

India

In contrast, Indian regulations do not have a defined biosimilars category. Rather, any biosimilars of a biologic that have been on the market for more than four years undergo an abbreviated approval pathway, whilst biosimilars of newer biologics must register as a “new” product. Additionally, the Drug Controller General appears to be the primary regulatory authority but approval from other agencies is also possible (Konski 2011).

Commercial Outlook

Commercial success of biosimilars is dependent on a number of challenges that have seen the relatively slow uptake of biosimilars compared with small molecule generics. There is a need to develop more effective approval pathways that provide adequate market incentives for biosimilar companies, whilst maintaining a balance with measures that ensure patient safety. Failing these, it is likely that companies will simply

shift their focus to developing 'bio-betters' (improved versions of an existing biologic) or new biologics. In this scenario, without the cost suppression from biosimilars, prices of biologics will remain high and limited patient accessibility will continue (Kanter et al. 2012).

A crucial aspect is the pricing of biosimilars. Biosimilars will not see the same level of discounts as generics of small molecule drugs, because of greater upfront costs associated with an expensive development and approval process. Whilst small molecule generics might be priced 80% lower than the brand name, biosimilars are likely to be priced at a lesser 20 to 40% discount (Senior 2013, Hirsch et al. 2013). However, we expect this discount will be greater in countries requiring less stringent regulatory steps, and as analytical technologies improve and the requisite for *in vivo* data is reduced (Senior 2013). Another challenge is that manufacturers of originator biologics may cut their prices to remain competitive and thus are capable in retain their significant market share (Hirsch et al. 2013). As price is the main driving factor, it is much more difficult for biosimilars to penetrate the market than traditional small molecule generics.

Just last year, McKinsey & Company (2013) published a white paper on the future of the biosimilars market. They commented that recent changes to develop more streamlined guidelines in emerging markets, particularly in the Central and South American nations, will permit companies to develop effective regional strategies for biosimilars. Additionally, incentives to boost local biosimilar development are evident, for example, in a biotech consortium of Brazilian pharmaceutical companies, as well as the Chinese government's investment in local biotech companies and partnerships with multinational biologics companies. This is coupled with relatively low degree of patent

protection in countries that have much smaller investments in original biologics, such as China and India (Table 1), who already have less expensive approval processes (Konski 2011). Table 1 shows the length of market and data exclusivity for original biologics. Data exclusivity describes the period during which any safety or efficacy of the original biologic cannot be used for comparison and thus the period during which regulatory authority will not accept new applications for a biosimilar. Entry into emerging markets may therefore be a valuable opportunity for biosimilar manufacturers, both as a source of early revenue and accumulating data for approval processes in more regulated countries.

However, safety concerns remain a barrier to greater acceptance of biosimilars. All biological products have the potential to cause immunogenicity, which can be life-threatening (Patel et al. 2014). However, even with recent advances in *in vitro* and complex *in vivo* models, these cannot always be predicted (Calo-Fernandez et al. 2012). There are well-documented examples of biologics which had DNA sequences completely identical to the human gene (e.g. erythropoietin) but demonstrated immunogenicity, whilst minimal immunogenic responses were reported for other biologics that had structural variations (e.g. IFN- α 2A) (Schellekens 2002). Thus regulatory authorities governing biosimilars still require intensive post-approval pharmacovigilance programs to monitor any differences in safety compared to the original biologic. It is interesting to note that Hirsch (2013) suggests that these current reporting and analysis mechanisms for biosimilars are not sufficiently effective and that more cost-effective pharmacovigilance programs are only recently beginning to develop. Nonetheless, only long-term experience with

biosimilars, well-defined guidelines and advancements in analysis systems will gradually earn the trust of clinicians and patients.

Table 1: Patent protection in major biosimilar markets for the original biologic in terms of exclusivity periods for market access and use of any original biologic data for biosimilar applications (Konski 2011)

Region	Market (years)	Data (years)
EU	10	8
USA	12	4
China	5	6
India	N/A	N/A

Conclusions

Biosimilars are expected to rapidly increase market share and economic relevance as more biologics reach patent expiry. This is reflected in recent activity relating to international regulatory legislation of biosimilars. Global and regional harmonisation of these guidelines is crucial for encouraging significant investment by biosimilar manufacturers. Nonetheless, these guidelines will evolve as new data and analysis technologies come into play. Safety data and experience with biosimilars with time are essential for regulatory agency, clinician and patient confidence. Despite various challenges, biosimilars will flourish in the near future due to the increasing financial burden on global healthcare systems.

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Associate Professor Daniela Traini is an ARC Future Fellow of the Respiratory Technology group at the Woolcock Institute. Her research covers all areas of respiratory research from bench to bedside.



The Royal Society of New South Wales



The Royal Society of New South Wales Awards for 2014

The Clarke Medal 2014

The Clarke Medal was established to acknowledge the contribution by the Rev William Branwhite Clarke MA FRS FGS, Vice-President of the Royal Society of New South Wales from 1866 to 1878. The Medal is awarded annually for distinguished work in a natural science done in Australia and its Territories.

The Medal is awarded by rotation in the fields of geology, botany and zoology. This year's award is in the field of Botany in all its aspects. Nominations are called for the names of suitable persons who have contributed significantly to this science.

The Council requests that every nomination should be accompanied by a list of publications, a full curriculum vitae, and also by a statement clearly indicating which part of the nominee's work was done in Australia and which part was done overseas. Agreement of the nominee must be obtained by the nominator before submission and included with the nomination.

The winner will be expected to write a review paper of their work for submission to the Society's Journal and Proceedings.

In cases where the Council of the Society is unable to distinguish between two persons of equal merit, preference will be given to a Member of the Society.

Agreement of the nominee must be obtained by the nominator before submission and included with the nomination.

Only electronic submissions will be accepted. Nominations and supporting material should be submitted by email (secretary@royalsoc.org.au) to the Royal Society of New South Wales marked to the attention of the Honorary Secretary, not later than **30th September 2014**.

The winner will be announced and the Medal presented at the Annual Dinner of the Royal Society scheduled to be held in 2015. The winner will be notified in December.



The Royal Society of New South Wales



The James Cook Medal 2014

The James Cook Medal was established in 1947 with funding by Henry Ferdinand Halloran. Halloran, who had joined the Society in 1892 as a 23 year-old, was a surveyor, engineer and town planner. He did not publish anything in the Society's Journal but he was a very enthusiastic supporter of research. Halloran funded what were to become the Society's two most prestigious awards, the James Cook Medal and the Edgeworth David Medal, the latter being the medal for young scientists.

The James Cook Medal is awarded at intervals for outstanding contributions to science and human welfare in and for the Southern Hemisphere.

The Council requests that every nomination should be accompanied by a list of publications, a full curriculum vitae, and also by a statement clearly indicating which part of the nominee's work was done in Australia and which part was done overseas. Agreement of the nominee must be obtained by the nominator before submission and included with the nomination.

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The winner will be announced and the Medal presented at the Annual Dinner of the Royal Society of NSW to be held in 2015. The winner will be notified in December.



The Royal Society of New South Wales



The Edgeworth David Medal 2014

The Edgeworth David Medal, established in memory of Professor Sir Tannatt William Edgeworth David FRS, a past President of the Society, is awarded for distinguished contributions by a young scientist.

The conditions of the award of the Medal are:

- The recipient must be under the age of thirty-five years at 1st January, 2014.
- The Medal will awarded be for work done mainly in Australia or its Territories or contributing to the advancement of Australian science.

Nominations are called for the names of suitable persons who have contributed significantly to science, especially the scientific aspects of agriculture, engineering, dentistry, medicine and veterinary science.

The Council requests that every nomination should be accompanied by a list of publications, a full curriculum vitae, and also by a statement clearly indicating which part of the nominee's work was done in Australia and which part was done overseas. Agreement of the nominee must be obtained by the nominator before submission and included with the nomination.

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The Royal Society of New South Wales



The Warren Prize 2014

William Henry Warren established the first faculty of engineering in New South Wales and was appointed as its Professor at the University of Sydney in 1884. Professor Warren was President of the Royal Society of New South Wales on two occasions. He had a long career of more than 40 years and during this time was considered to be the most eminent engineer in Australia. When the Institution of Engineers, Australia was established in 1919, Professor Warren was elected as its first President. He established an internationally-respected reputation for the Faculty of Engineering at the University of Sydney and published extensively, with many of his papers being published in the *Journal and Proceedings of the Royal Society of New South Wales*.

The Warren Prize has been established by the Royal Society of NSW to acknowledge Professor Warren's contribution both to the Society and to the technological disciplines in Australia and internationally. The aim of the award is to recognise research of national or international significance by engineers and technologists in their professional practice. The research must have originated or have been carried out principally in New South Wales. The prize is \$500.

Entries are by submission of an original paper which reviews the research field, highlighting the contributions of the candidate, and identifying its national or international significance. Preference will be given to entries that demonstrate relevance across the spectrum of knowledge – science, art, literature and philosophy – that the Society promotes.

The winning paper and a selection of other entries submitted will be peer-reviewed and are expected to be published in the *Journal and Proceedings of the Royal Society of New South Wales*. Depending on the number of acceptable entries, there may be a special edition of the *Journal and Proceedings* that would be intended to showcase research by early- and mid-career Australian researchers.

Only electronic submissions will be accepted. The paper should be submitted by email (secretary@royalsoc.org.au) to the Royal Society of New South Wales marked to the attention of the Honorary Secretary, not later than **30th September 2014**. The manuscript will be passed on to the Editor of the *Journal* for peer review.

The winner will be announced and the Medal presented at the Annual Dinner of the Royal Society scheduled to be held in 2015. The winner will be notified in December.



The Royal Society of New South Wales



The Royal Society of New South Wales History and Philosophy of Science Medal 2014

The Royal Society of NSW History and Philosophy of Science Medal was established in 2014 to recognise outstanding achievement in the History and Philosophy of Science. It is anticipated that this prize, like the Society's other awards, will become one of the most prestigious awards offered in Australia in this field.

Persons nominated will have made a significant contribution to the understanding of the history and philosophy of science, with preference being given to the study of ideas, institutions and individuals of significance to the practice of the natural sciences in Australia.

Entries may be made by nomination or direct submission. All entries should be accompanied by a full *curriculum vitae* and include a one-page statement setting out the case for award. In the case of nominations, the agreement of the nominee must be obtained by the nominator before submission and included with the entry.

The winner will be expected to submit an unpublished essay, drawing on recent work, which will be considered for publication in the *Journal and Proceedings of the Royal Society of New South Wales* during the following year.

Only electronic submissions will be accepted. Nominations and supporting material should be submitted by email to the Royal Society of New South Wales, marked to the attention of the Honorary Secretary (secretary@royalsoc.org.au), no later than **30th September 2014**.

The winner will be announced and the Prize presented at the Annual Dinner of the Society to be held in 2015. The winner will be notified in December.



The Royal Society of New South Wales



Royal Society of New South Wales Scholarships 2014 The Jak Kelly Award 2014

The Royal Society of New South Wales is the oldest learned society in Australia, tracing its origins to 1821. It has a long tradition of encouraging and supporting scientific research and leading intellectual life in the State. The Council of the Society funds the Royal Society of New South Wales Scholarship in order to acknowledge outstanding achievements by early-career individuals working in a science related field.

Applications for Royal Society of NSW Scholarships are sought from candidates working in a science-related field in New South Wales or the Australian Capital Territory. There is no restriction with respect to field of study. Up to three Scholarships will be awarded each year. Applicants must be enrolled as research students at a university in NSW or the ACT on 1st July in the year of the award. Applicants must also be Australian citizens or Permanent Residents of Australia.

The Jak Kelly Award is awarded jointly with the Australian Institute of Physics to the best PhD student talk presented at a joint meeting with the AIP.

The awards consist of certificates acknowledging the achievement, a \$500 prize and a free one-year of membership of the Society. The winners will be expected to deliver a short presentation of their work at a Meeting of the Society in 2015 and to prepare a short paper for the Society's Journal and Proceedings.

Applications must include

- 500-word summary of the work.
- Statement of the significance of the work, particularly within the broader context of your chosen field.
- Curriculum vitae, including details of their research candidacy.
- Letter of support from your research supervisor.

Applications should be submitted by email (secretary@royalsoc.org.au) to the Royal Society of New South Wales marked to the attention of the Honorary Secretary, not later than **30th September 2014**. The winner will be notified in December.



Archibald Liversidge: Imperial Science under the Southern Cross

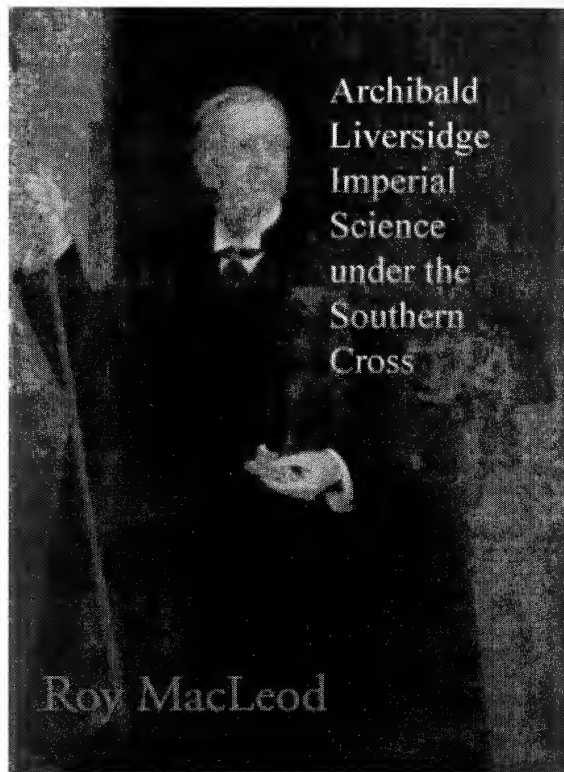
Roy MacLeod

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When Archibald Liversidge first arrived at the University of Sydney in 1872 as Reader in Geology and Assistant in the Laboratory, he had about ten students and two rooms in the main building. In 1874, he became Professor of Geology And Mineralogy and by 1879 he had persuaded the University Senate to open a Faculty of Science. He became its first Dean in 1882.

In 1880, he visited Europe as a trustee of the Australian Museum and his report helped to establish the Industrial, Technological and Sanitary Museum which formed the basis of the present Powerhouse Museum's collection. Liversidge also played a major role in establishing the *Australasian Association for the Advancement of Science* which held its first congress in 1888.

This book is essential reading for those interested in the development of science in colonial Australia, particularly the fields of crystallography, mineral chemistry, chemical geology and strategic minerals policy.



To order your copy, please complete the form Liversidge Book Order Form available at:

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